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CHILDREN'S REACTIONS TO MOVIE HORRORS AND RADIO CRIME

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BEING startled many times by the terror inspired in children by motion pictures and radio programs, the writer studied the reactions related by 200 children, normal physically and mentally, in the responses given to an emotional inventory which had been designed to detect maladjustments shown in the various aspects of child life, and, in so doing, was struck by the number of phases revealed which would be of interest to pediatricians. A full history of each child had also been given by the parent.

There were 120 boys and 80 girls in the series, from 6 to 16 years of age. To afford a better number for comparisons of physical effects, the last ten of the consecutive cases were dropped and their places filled by ten additional children who had subsequently happened to come into clinic or private practice by the time of writing, and whose lot it had been to escape "bad" movies and radio entirely. This raised the total of fortunate children to forty-seven, a group which proved to be fairly homogeneous in reaction. The descriptive word "bad" has been adopted from the children's vocabulary, evidently meaning to them those with a bad effect; some used "scary" in the same way. In this group of forty-seven, three boys and four girls had never seen a movie (one of 8, three of 9, one of 11, and two of twelve years). Ten did not see a movie until 10 to 13 years of age (three of 10, two of 11, two of 12, and three of 13 years). Twenty-nine had no bad movies or radio programs in their experience, and one saw no bad movies until after twelve years of age. In addition to the forty-seven mentioned, there were also four who had seen only good movies but who were addicts of radio crime programs.

In classifying groups, the word "addiction" has been used in the medical sense, as giving oneself over to a habit-forming practice very difficult

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to overcome, no matter how the aftereffects are dreaded. With this in mind, the addiction was divided into three classes: severe addiction (movies two to five times a week and many of the crime programs); moderate addiction (movies one to two times a month and one to two serious crime programs like "Calling All Cars," "Gangbusters," "Behind Prison Bars," etc.); mild addiction (several times a year and milder crime programs like the "Lone Ranger"). In most cases, the degree of radio addiction matched that of movie attendance, although there were twenty-three who were allowed to see bad movies but restricted to good radio programs; while, on the other hand, there were the four mentioned who saw only good movies but listened to the worst radio programs. This grouping gave 114 (57 per cent) as severe; twenty-five (12 per cent) as moderate; and fourteen as mild, including the four with the bad radio only. The forty-seven nonaddicts complete the number of 200.

In general, it was found that movies and radio serve not merely as recreational outlets, often used because of lack of resources within the family life, but that among given layers of society, movie attendance, like the possession of an automobile in higher layers, definitely bestows social prestige; the more a family can go, the higher the social status. The number of radios owned is stated proudly, especially if each parent and each of the two or three children owns one. In certain social layers, the children on Saturday or Sunday, or both, are dressed in their best, given from five to twenty-five cents for candy, and sent off early to parade up and down the aisles and from seat to seat, ostentatiously licking the candy and holding it so all may appraise its value. One wonders how the old Sunday school attendance has fared. Even at school, children lose face if they cannot discuss the hair-raising details or act out the goriest murders on the playground. Then, too, getting the children from under foot by parking them in a show gives marked relief in small living quarters, especially if they stay from noon until dark, as is not uncommon. In poor families, on or off relief, in which a radio, shows, and permanent waves seem to be considered necessities (although those at the lowest end of the self-respecting, self-supporting populace are largely deprived of them), the whole family is dragged along to the movies, since there is no money left to pay for someone to stay with the children at home. Nor can Father be denied his thrills from crime programs, even if they penetrate every nook of the small apartment until after 11 at night. Movies and radio seem to have sapped the family resources for entertainment; games, handiwork, reading aloud, and so on, seem unknown relics of the horse-and-buggy days.

Naturally, the effects of addiction were found to vary in different children, whether expressed by the general health, nervousness, sleeping, eating, thinking, fears, and so forth, or with an overlapping of fields. Neutralizing agents were found to be a good physique, a comforting

security in the home, a satisfying relationship with one's own fellows, and a desirable success in the school world. A powerful factor in intensifying the effects of movie horrors and radio crime is the ability of the child to take on the action he is seeing or hearing as his own, by sympathetic participation in the experience of the screen or radio person. That there is vicarious indulgence in love by women and in sports by men is common knowledge. In their dreams and fears, children disclose that they, too, partake in varying degrees in the activities portrayed, and, as later examples will illustrate, the victim seen or heard in the terrifying situation becomes the self and the other victims become the members of the family, as the scene is relived. To represent what the child's mind does with the indigestible mass forced into his mental craw, the following dreams of 9-year-olds are given:

1. "I see snakes and spiders in the dark like those in the movies and they let a poison snake loose on a train from a box and it bit a man and he died."

2. "I often dream crocodiles are all around me and after me and I have to jerk and jerk all over the bed to get loose from them."

3. "I dream most of 'Clutching Hands,' where the window opened very slowly and a lot of hands came in and kept clutching until they got to the lady's neck and choked her and then pulled her out of the window and it felt like me. I always dream mostly about dead ones like those they drug over and pressed a button and threw them down a cave."

4. "My last dream was about training lions in Africa for my circus and some bad men came and gave them dope and then they killed me."

5. "I dream mostly of choking girls' necks."

6. Little girl: "I dream about tribes of black men that catch a pretty girl in a trap but a white tiger comes and eats her up and I think it's me."

7. "I've dreamed many times that they caught me and put me in the electric chair like in 'Angels With Dirty Faces.' And I've screamed and screamed over it and in the 'Haunt Came Back.'"

General Health.—While notes had been taken as to the state of nutrition, color, physique, and the rest, and this had been combined with other information in the questionnaire and from the parents, the evidence was too indefinite to tabulate, although it seemed to give the nonaddicts a 35 per cent lead in satisfactory health conditions. The following excerpts show that a general effect can follow the arousal of emotions:

1. Nine-year-old girl: "I always scream if they knife somebody. Sometimes I get so scared my stomach hurts. In the night I know someone is coming in the back window, the way they do in shows and I can hear someone creeping around the room in the dark. There is always skeletons in the corners. I get excited when there is a war picture and I say to myself, 'Get 'em, boy; get 'em, boy.'"

2. Eleven-year-old boy: "I worry that strangling might happen to me. I know a boy and a kidnapper chased him all the way home and he was so scared he was sick in bed for days."

Nervousness.—This was judged by objective evidence during the hour's interview with the child. The extreme degree of nervousness was distressing to witness; some were shocking. At times a desire would arise to throw a switch of some kind to cut off the numerous jerks, twitches, and ties, in order to have a breathing spell during the hour.

A total of 116 of 153 addicts (76 per cent) showed more than ordinary nervousness, while nineteen of the forty-seven nonaddicts (40 per cent) did, an improvement of 36 per cent for nonaddiction. Of the 116 addicts, sixty (52 per cent) showed +++ nervousness as against two of the forty-seven nonaddicts (4 per cent), a lead of 48 per cent for nonaddiction. Thirty-two of these addicts (28 per cent) showed ++ nervousness, as against four of the forty-seven nonaddicts (9 per cent), a lead of 19 per cent. Of the sixty with +++ nervousness, thirty-nine (65 per cent) were severe addicts, while of the thirty-two with ++ nervousness, seventeen (53 per cent) were severe addicts. Excerpts, one for each age group, follow as illustrations:

1. Seven-year-old: "I always wring my hands at movies. I've got a radio of my own and I can listen to all the police calls."

2. Eight-year-old: "Sometimes I shake all over and my hands jerk and I bite my nails way down when radio or movies are bad."

3. Nine-year-old: "I get scared at the radio and I bite my nails and when there is shooting, I shiver and shiver and jump on the chair and fight with my hands and run to the window to see if it's coming. I get very nervous, excited. Spooky things on the radio make me too much of a scaredy and when Papa comes in, I think he is a ghost and I run and fell over the chair and broke the top and Mama say, 'Who break this chair,' and I say, 'Mama, will you hit me if I tell you?' "

4. Ten-year-old: "Spooky ones are best and gangsters are really good but I hate love ones. When I saw 'Dracula's Daughter,' I jumped right up and yelled out in it and had nightmares nearly every night after."

5. Eleven-year-old: "I can't go to shows at night, because I can't sleep afterward. I get too excited and nervous anyhow when the crooks start shooting."

6. Twelve-year-old: "Oh, gosh, but I get jolted by mysteries! I am a nervous wreck afterwards—spookies the same. Killings get me awful nervous. When I listen to 'Gangbusters,' I get all jittery. I still have nightmares and, if I am alone, there is always a robber in the house and I know he will jump on me if I go in the kitchen. Men are always creeping up on me in the bathroom and when I am going to sleep, I know that the crooks are under the bed."

7. Thirteen-year-old: "Some movies make me so nervous and jittery, I forget my way home."

Sleeping Disturbances.—These were easy to gather as the children attach no importance to their night terrors, nightmares, and night walking. Nor did they mind telling their fears in the night to a noncritical, sympathetic person. Becoming so terrified that they had to go to the mother's bed or screaming from fright until the mother had to waken them were common reactions up to 12 years of age. The other very common reaction occurring at almost any age and interfering with sound sleep was that of pulling the covers over the head, burying the head under the pillow, or diving under the covers clear to the foot, with or without pillow, there to spend the night. With oxygen intake so restricted, one wonders how refreshing such sleep can be, to say nothing of the effect of the night terrors, night walking, and nightmares recorded.

A total of 130 of 153 addicts (85 per cent) showed sleep disturbances, as against nine of forty-seven nonaddicts (19 per cent), apparently an unnecessary, preventable 66 per cent of sleep disorders. Of the 130 disturbed sleepers in the addicts, 105 were disturbed to a ++ or +++ degree (81 per cent), as against five disturbed sleepers in the nonaddicts (11 per cent), a difference in favor of nonaddiction of 70 per cent.

The following are excerpts illustrative of sleeping disturbances at each age level:

1. Seven-year-old: "After a spooky, I dream a lot and wake up and can't go to sleep and have to get out of bed and go to Mother."

2. Eight-year-old: "Ghosts and robbers, like in the show, seem to be around me when I am alone and I have to put my head under the pillow and go to the bottom of the bed; and I hear the closet door open and men with guns and kidnappers creep around. I dream such bad dreams that they wake me up and I have to go to Mother's bed, but I've got used to murders now but I still dream of people getting killed in crashes and everything going red."

3. Nine-year-old, a dainty, little girl: "I have dreamed millions of times of people getting hurt, killed, shot, hit over the head or stabbed. My last dream was that the neighbor lady went home and found her husband in a closet with a knife in him. I have terrible dreams. It's awful."

4. Ten-year-old: "The worst movie I ever saw was about a lady with smallpox and she went around and gave it to everybody and you saw them die. When I am alone, I think of how thieves take children in the movies and I don't know what to do. In the dark, I see eyes looking at me and men with guns and big dogs and a man stands in the door and I feel somebody under the bed and there is a noise in the closet. I have to lie awake a long time."

5. Eleven-year-old: "I go to shows two times a week, sometimes more. I kick and talk in my sleep afterwards and have to sleep with Mother because I walk in my sleep so much. I can't go to the movies at night because I can't sleep afterwards. I hate war and spooky pictures and

get too scared when it's like the 'Slave Ship' and the 'Old Soak.' I still dream about the one I saw four years ago where the man cut the lady's head off and carried it around. I dreamed a long time about the woman who came up out of the ground and killed people. I usually dream of a lady and men killing, the drunken type, you know. I had one dream I dreamed over and over about a guy that cuts heads off. I had to think of that in the daytime, too, it made me feel so leery and scared. I sometimes see a lady or a man dying in my dreams.

6. Twelve-year-old: "I couldn't sleep for several nights after the 'Mummy' and the 'Invisible Ray,' and I was scared in the daytime for fear the guy in the 'Invisible Ray' was doing things in my house."

Eating Disturbances.—These data are the least accurate, as mealtime has become a highly charged battleground with fusillades and bombardments of arguments, culled largely from high pressure advertisements and pseudopsychologists' warnings not to correct the child at the table or digestion will stop instantly. The children were on their guard; some little prigs said their favorite food was spinach but capitulated over a choice between ice cream on one hand and spinach on the other. Otherwise, the children delighted in naming their pet aversions to food, what mother had to coax them to eat, and what she fussed about anyhow. (What a relief it would be if feeding could be regarded only as a refueling process or merely one of stoking the engine!) Some mothers complained of the effects of the noon crime programs on their children's appetites.

There were eighty-two of the 153 addicts (54 per cent) who showed eating disturbances, as against thirteen of the forty-seven nonaddicts (28 per cent), a difference of 26 per cent in favor of nonaddiction. Of these eighty-two showing eating disturbances, fifty (62 per cent) were severe addicts.

An example of the effects of terror in eating is this statement by a nine-year-old boy: "Sometimes I dream after a jungle picture that two men jump out behind me from the jungle and they keep pulling till they pull me right apart and put me in the fire and I feel sick as a dog when I wake up in the morning and can't eat at all."

Fears.—Parents frequently express indignation that their children have not volunteered the content of their fears and bad dreams to them (and so cut off the source of their fascinating addiction). The younger ones make no bones about telling them to an understanding person with no authority over them. The older ones often had to be approached indirectly, as in the past tense using such questions as "What did you used to think of while going to sleep?" "What did you fear if you were alone?" "What dreams have you had of death?" and then be led on to the present.

There were 144 of the 153 addicts (94 per cent) who suffered from fears, as against eight of the forty-seven nonaddicts (17 per cent), a

difference of 77 per cent. Of the sixty (42 per cent) with extreme fears, forty-three (71 per cent) were severe addicts, while none of the nonaddicts showed extreme fears. Of the sixty-four (44 per cent) addicts with ++ fears, thirty-nine (61 per cent) were severe addicts, as contrasted with two nonaddicts (4 per cent) with ++ fears, a difference of 57 per cent. It was interesting to discover how those fared who had not been protected from bad movies but had been from bad radio, and also the four allowed bad radio but no bad movies. Of the twenty-three with bad movies but good radio, five had extreme fears (22 per cent), a lessening of 20 per cent; eleven had ++ fears (48 per cent), a not significant difference. This regime had helped, but not enough. Two of the four radio addicts who were protected from bad movies, but who were also rejected at home, showed extreme fears and two ++ fears. The exciting radio program heard just before bedtime is continued in sleep, of course, and is thus very effective in contributing to bad dreams and fears.

Many children take a morbid interest in comparing notes on "awful" details striking terror into their hearts, especially when they are helpless to prevent inner identification of themselves, and sometimes their families, with the victims of the plot, which again adds more fears and keeps them fresh in memory.

1. Six-year-old: "I dream about a million of clutching hands and about taking eyes out and rats bite a boy and poison him. Sometimes there's two skeletons hanging from a tree and a man drags them up and puts them in a room and cuts the boy's head off and puts his hair on the tree and it looks like my head."

2. Seven-year-old: "When I wake up in the night, I see skeletons walking around leaving black marks and I hear footsteps and windows being opened softly."

3. Eight-year-old: "Gee, I've had plenty of dreams about the man they dipped in hot wax and the big spider that ate up men. He tore his flesh right off his ribs and everything. After shows I mostly see a gangster hiding behind the chair and I can hear him whisper and walk around and open the window and I duck my head under the covers and go clear to the bottom and lie crossways."

4. Nine-year-old: "Lots of times I dream of people sneaking in and sticking knives in me. Then I dream that Father had poison like in the movies and he died. My last dream was how Frankenstein took my mother and threw her in hot mud and the steam comes up and it burns people awful. When I wake up in the night, I see lots of faces like in the show and men mostly getting Mother kidnapped in an auto."

5. Ten-year-old: "There was a storm I dream about and the octopus that reaches out all his arms and gets you."

6. Eleven-year-old: "The worst I saw and dreamed about was an operation where they cut an artery too short."

7. Twelve-year-old: "After I've been to a bad movie, I try to be brave but I can't do it very well. In the dark I feel a knife behind me like in the show. I keep dreaming that the giants in the show take my mother and father and my dog and change the folks into fat toothpicks and put them through the grinder with the dog."

8. Thirteen-year-old, a fine looking, friendly boy: "When I saw Charlie Chan, I couldn't stand it so I got out and, when I got out, I was too scared to go home."

Nail Biting.—Using nail biting as a symptom of strain and stress occurring under various conditions, data were compiled which showed that nails were bitten by seventy-eight of the total 153 addicts (51 per cent), while eleven of the forty-seven nonaddicts did likewise (23 per cent), a difference of 28 per cent.

Terming as worst addicts those attending movies two to five times a week and listening to practically all crime radio programs, a comparison was made between the worst addicts (sixty-one), the rest of the addicts (fifty-three), and the nonaddicts (forty-seven), as to nail biting. It was found that among the thirty-one worst addicts who were nail biters, there were eighteen (60 per cent) who bit their nails only during movies, radio programs, or both, while eighteen of the rest of the addicts (38 per cent) did likewise. With the nonaddicts, three of the eleven nail biters (27 per cent) reported nail biting even when listening to good movies and radio. This gives a total of thirty-nine of the eighty-nine nail biters (43 per cent) who bit their nails during movies, radio programs, or both.

School was also noted as a place for nail biting, probably indicative of thinking difficulties in these children of normal intelligence, a reflection either of the condition of their nervous systems making it difficult for them to concentrate, or of the inadaptability of the school program to individual children, or possibly both. Twenty of the nail biters bit their nails only at school and nine both at school and during movies, radio programs, or both, making a total of twenty-nine of the eighty-nine nail biters (33 per cent) who had become nervous enough to bite their nails over the school situation, even though they were intelligent, thus registering insecurity in the school field. The rest of the nail biters, twenty-one (24 per cent), bit their nails at any time.

1. Seven-year-old: "No, I don't bite my nails" [hiding them from view; very little of them left]. They get like that when I listen to the radio but I wouldn't bite them ever."

2. Eight-year-old: "'Gangbusters' is my favorite program and I bite my nails way down thinking about it when I'm in bed."

3. Nine-year-old: "I bite my nails when I listen to 'Gangbusters,' 'Calling All Cars,' 'Court of Human Relations,' and others, and when I am going to sleep, I am the guy that goes on catching crooks."

4. Ten-year-old: "I bite my nails so much at shows that mother makes me chew gum instead. I bite them during the radio, too, if father is not watching me."

5. Eleven-year-old: "All the family listens to 'Drums,' 'True Detective Stories,' 'Calling All Cars,' 'Gangbusters,' and the rest. I think about them when I am going to sleep and I bite my nails when I hear them moving around and see a bandit climbing in the window."

6. Twelve-year-old: "When I am at the show I bite my nails. I jump out of my seat every time they shoot. My father likes the bad radio programs."

7. Thirteen-year-old: "I have to listen to the crime programs with Father and I bite my nails and I can't go to bed till after 10."

8. Fifteen-year-old: "I don't know when I bite my nails at the movies and listening to the radio but they get bitten clear down."

Other Reactions.—In studying the records of the sixty-one worst addicts (movies two to five times a week and practically all of the worst radio programs), nine girls were found whose reactions did not conform to those shown by the others, or to a much less degree, or by fewer phases. Of these nine, six were found to be in training for motion picture appearance, and were largely able to regard otherwise alarming actions from the viewpoint of a fellow actress, which, however, did not save them from all deleterious effects. These girls had a sophisticated attitude and were very self-centered in outlook and interests; the ordinary child world was brushed aside as unworthy of notice.

The other three girls were adolescents, engrossed with love to the exclusion of other emotions as they moved like somnambulists through the dense love haze that enveloped them. Even the persecution of a mean stepfather, in one case, failed to penetrate the haze with the customary sting. Several others did not reflect the usual strain either. These were older boys, big six-footers, who could remember, with an effort, all the common, fearful reactions in the past, but who had experienced such a tremendous upsurge of growth, vitality, and strength with their adolescent development that no day was long enough for the sports and other activities and interests in which they were now able to participate with success, to their deep joy. However, some of these were so carried along with the tide of restlessness and excitement that they demanded the most gruesome of murders, the utmost refinement of torture and cruelty, and so forth, to satisfy their intense craving for thrills. These will be discussed later.

By contrast, the amount of disturbance shown by the nonaddicts seemed ridiculously small, but it was remembered that the history taking of the fears, dreams, and disturbances in nonaddicts was a dull performance at best, with very little interesting material unearthed, so much so that the first few nonaddicts were thought to be holding back, but this

did not prove true in the rest of their questionnaires and the dullness recurred with monotonous regularity throughout the series.

Radio Crime Before Bedtime.—Of course, in the majority of cases, radio crime cannot be considered independently of movie crime. The two are inextricably mixed. Both deal with the same crime situations. While radio could be said to lack visual stimulation, it does not work out that way, since the vivid movie scenes of similar situations flash into mind instantly as soon as mentioned on the radio.

The average child radio addict starts lapping up his fascinating crime at about 4 o'clock in the afternoon and continues for much of the time until sent to bed. The spoiled children listen until around 10 o'clock; the less indulged until around 9 o'clock. Of course, asking the child, or even at times the mother, when he goes to bed will not elicit this information. The easiest way is to ask the names of the programs listened to and then consult newspaper programs as to time. Some children are guileful enough to announce in an innocent tone of voice that they are in bed at 7:30, which is true enough, but what they neglect to add is that nobody in the home can escape any word from the radio when Father or Big Brothers break the monotony of their drab existence by the loudest blood-and-thunder they can manage. As was said before, Mother plays a part in the addiction also. There is nothing so miraculous as exciting radio programs in keeping the children quiet and "out from under foot" when in the home, so Mother continues to feel guilty about allowing them to hear "such dreadful things," but "everybody does it" and her hand is stayed. The children who come home for lunch have an added crime treat on the radio while eating, digestion to the contrary notwithstanding. Words fail when it comes to expressing an opinion on the increasing practice of giving a radio to a child for his own use and thus giving him a choice of programs, sleeping hours, and use (or rather, abuse) of play and social times; the children's reports will have to speak for themselves on this.

Everyone has noticed that if he takes his troubles to bed with him, or allows himself to brood over his worries or anxieties before dozing off, these same troubles, worries, and anxieties have a way of breaking through restful sleep into a state of semiconsciousness where they continue to hound and harass the defenseless mind by assuming most bizarre forms as fantastic dreams warranted to abolish all the refreshing effects of sound sleep. From the children's reports, the brain functions exactly in the same way when the mind is filled with movie horrors and radio crime before sleep. As a result, we are confronted with a situation of crime and horror uppermost in the child's mind from about 4 P.M. daily as a usual routine until bedtime, and after that continuing to interrupt restful sleep during the night. This uppermost position is again assumed when notes on terrifying aspects are compared with other addicts at school recess and noon, while fascinating plots are acted out after

school, to say nothing of what happens when the schoolroom work becomes dull and drab and all that is needed for relief is to punch a mental button to revive the vivid, thrilling film or plot. Each repetition of the crime in memory serves to deepen the original impression toward permanency.

Of the addicts, 85 per cent admitted listening to radio before going to bed and continuing to think of it on going to sleep. Not only that, but the next step turned out to be that of thinking of the self as the crook committing the crime, and finally progressing to the plane of planning the crime, acting it out, studying the faults of the plan, and rectifying them in the next plan made—in short, a long-continued study in being a criminal. One of these boys, 11 years old, had already acquired three real guns—a pistol, a repeater, and a six-shooter. That movies can have a similar effect was brought to mind when the writer inadvertently had to sit through a cowboy scene with much shooting in it. Not only was the audience largely composed of children from 3 years old and up, but a goodly number were armed with toy guns and every time a man was shot, whether cop, crook, or cowboy, each child's gun was aimed at the man on the screen, with a tense expression, each shooter said, "Bang," and then looked satisfied and proud if the man fell. If this is not training to kill, what is it?

1. Seven-year-old: "In the night I think of the cops and robbers on the radio and then the cops blame me and chase me."

2. Eight-year-old: "All of the family listen to 'Sing Sing,' 'Calling All Cars,' 'True Detective Stories,' and like that, but a doctor said I shouldn't listen to them any more so I don't stay in the room but I can hear from my bed."

3. Nine-year-old, a pretty little girl: "Oh, but I do love radio mysteries! Oh, Gee, I love 'em, even if I dream of them. I undress slowly so as not to miss any of them [all the worst]."

4. Ten-year-old: "I like to listen to the radio program when I eat my lunch. It's exciting. There's shooting in it."

5. Eleven-year-old: "I have my own radio in my room and I listen to 'Drums,' 'Sing Sing,' 'Calling All Cars,' 'Gangbusters,' and others. I think it all over when I try to go to sleep and it takes me quite a long time because I hear doors opening and guys under my bed and men with guns and I tuck my head under the covers and go clear to the foot of the bed. I can't read but I like the pictures in the 'big-little' books about detectives and shooting."

6. Twelve-year-old: "I don't like to play with children any more since I have my own radio. I don't like to have my friends come in—my good times are with the radio. I start listening as soon as I get home from junior high and I listen until dinner time."

7. Thirteen-year-old: "When I'm going to sleep after the radio, I plan out crimes and then plan the best way to catch the criminals and then make a better plan."

8. Fourteen-year-old: "I like to think how I would have done in the crook's place when I am going to sleep."

9. Fifteen-year-old: "Mother's the one who likes crime in our family and we all hear it."

Callousness.—As was mentioned before, the highly seasoned, indigestible movie and radio fare has developed an ever increasing appetite for an overstimulating mental diet until an orgy is demanded for satiation. More than that, it was found that hundreds and hundreds of exposures to the sufferings of others for the purpose of entertainment most unfortunately have brought about, in many, many children, an atrophy of such desirable emotions as sympathy and compression toward those in distress, and also of the desire to help or alleviate the pain or misery of those being hurt or maltreated, even to the point of torture. The troubles of others were found to become stage scenes of no more personal concern beyond entertainment than the props used in the film settings. This atrophy leaves scar tissue in the form of a hardness, an intense selfishness, even mercilessness, proportionate to the amount of exposure and its play on the native temperament of each child. Resentment to insults, indignities, and even cruelties to helpless old people, women, and children disappears. "It used to make me want to fight them when they did it but it doesn't any more." Altruistic impulses not followed by appropriate actions soon become sterile and nonexistent. It is easy to reason out that this is a natural sequence, but to hear small children voice this callousness still strikes a jarring note, while the blasé attitude of the older ones continues to cause a reaction like that of sand rubbed under glass. The writer has been unable to build up an immunity to either, but rather an increased susceptibility to the significance as the hopelessness of the situation continues.

1. Eight-year-old: "I used to dream about killings but I'm used to 'em now."

2. Nine-year-old: "I used to holler and holler after shows and couldn't sleep, but now nothing at all can have any effect on me." (Shows three times a week.)

3. Ten-year-old: "I don't mind killings now even when they are sawed up."

4. Eleven-year-old: "I don't mind dying now if they do it right away."

5. Twelve-year-old, a girl: "I used to get scared but I love them now and thrive on them. I really enjoy bloody ones and don't mind stabbings and killings at all."

6. Thirteen-year-old: "I only like shows where they are really exciting now. It doesn't make any difference to me if slaves get whipped to death or people stabbed. I don't care about any suffering if it isn't me."

7. Fourteen-year-old: "The way detectives handle cases is the most interesting part. I don't feel pity unless it's very bad. But in a way I would rather not watch them die."

8. Fifteen-year-old: "I don't care if people get hurt and I don't feel pity for them any more when they suffer. It's not so exciting if there isn't something like that. I get tired of the tame ones and want them with new excitement."

Dreams of Killings.—The terrific impact of violent death on the child's susceptible mind was indicated by the 74 per cent of the addicts who talked about it. These deaths are termed "killings" by the children, and again identification of the self in the horrifying murder scenes is seen to occur.

Closely allied to the fears of killings in addicts are those of death in the family if there is any sickness present at all, which is hardly surprising when the spectacle of death is so forcibly and frequently brought to mind. To some it was too much for them to admit, although their reactions strongly indicated emotional disturbance; others could nod but not talk; thirty-seven per cent could admit it. Children are unable to judge the seriousness of an illness in the family or even what sickness is, and tend to magnify to the danger point any sickness, even colds and headaches. This is true especially of children who are insecure in the home (about one in five or six). So great is the need of these children for love and security that a haunting fear lurks in the back of their minds that Mother may be lost to them entirely, that she may have been taken to the hospital and won't be home after school and may "never come back at all." Film scenes which depict dying keep this fear alive.

1. Seven-year-old: "Oh, boy, but shows are good, even if there's killing! I dream about a lady who has a elephant kill people for her. When I see men with guns in the dark, I grab the knife I keep under my pillow and get ready for them. I dream that lots of guys are getting shot and blood comes out of their heads and sometimes people getting whipped till they are dead."

2. Eight-year-old: "I dream of me getting killed and little girls getting killed and of robbers and shooting and stabbing and I never can call or run, I'm so frightened."

3. Nine-year-old: "All the time I dream about me getting knifed or shot or killed and robbers getting me and kidnappers pulling a sack over my head and me dying trapped in a cage with a tiger."

4. Ten-year-old: "Most of my dreams are about killings and sometimes it's Mother's head that is being chopped off. Then I can't get to

sleep again and I say, 'I'm getting a pill, I'm getting a pill,' twenty thousand times before I can get to sleep."

5. Eleven-year-old: "I dream a lot and I don't like it—they are always trying to kill you with guns and animals and things."

6. Twelve-year-old: "I am always dreaming bad dreams about me getting electrocuted or stabbed."

7. Thirteen-year-old: "My last dream was about a soldier that they killed and then he kept right on fighting like in the show."

8. Fourteen-year-old: "I've dreamed many times of a man who had his head chopped off and it seemed to be me sometimes."

Kidnapping Fears.—These were a strange mixture of hearsay, warnings, and terrifying conceptions from movies and radio, as told by 78 per cent. It was early discovered that many of the children had individually worked out an especially horrifying plan of which they lived in dread. The reality of these fears was often demonstrated by the deep sigh and hopeless slump that followed the recital of even the most fantastic, sometimes winding up with a naive remark such as "And I don't like to be burned up," sometimes plaintively, sometimes resentfully, and sometimes querulously given.

In the nonaddicts, kidnapping fears were lacking in twenty-four (45 per cent); the rest said they had been given some warning by their parents, but it had evidently been sanely given because they said they seldom thought of it and only heard talk when there was a recent case of kidnapping. With no frightful mental pictures from movies or radio impressed on the suggestible minds of these children, their parents were able to reassure them as to their safety, while no words could reassure them or overcome the harrowing scenes of movie and radio.

1. Six-year-old: "I know a gangster will tie me to a chair and leave me until he robs the bank and there's a man walks up our street with bags and everybody knows what's in them. He says, 'Come into the car and I will give you some candy.' "

2. Seven-year-old: "I have to watch out for kidnappers when I go alone at night to the show. There was a boy killed after a show. They lay out ropes on the sidewalk and you step in and you get jerked and caught. I dream about it."

3. Eight-year-old: "When I think I hear kidnappers coming, I open the pocket knife I keep under my pillow and hold it ready. I think they will put the pillow around my head and take me off in the car to the desert or forest before they kill me."

4. Nine-year-old: "At night kidnappers hide and they sneak in and hold your mouth and put you in a car and go away and into a shack and leave you there and tie you up and put the house to fire."

5. Ten-year-old, a girl: "I often dream of me getting kidnapped with a live wire that one man holds with electric gloves and the other man waits to catch me."

6. Eleven-year-old: "When I'll be kidnapped, I would be on the street and they would get me into the car and take me off and kill me by burying me alive and I don't like to be buried alive."

7. Twelve-year-old: "There's a house next door and I fear that the kidnapper will climb up to the bathroom window and get in and take a hypnotic needle and put dope in my arm and if there is no ransom, he will kill me and throw me into the river with cement."

8. Thirteen-year-old: "Kidnappers will come in the window and take me off and shoot me down a buzz saw into a mill."

9. Fourteen-year-old: "I watch out that somebody that's insane doesn't come in and get me."

Daydreaming in School.—Finding children's thoughts off in crime clouds much of the time led to questioning as to what passed through their minds when doing nothing or when tired of their work in school. Sixty per cent of the addicts answered that they daydreamed in school of the most exciting of the movies and radio programs: the lovelorn, of sensuous love-making scenes; the would-be cowboys, of thrilling round-ups and shooting; while most of the addicts gloried in lurid details of breath-taking crime sugar-coated as crime prevention efforts. The equipment furnished teachers with which to make impressions or hold the attention of pupils is skimpy at best, while movie magnates have almost unlimited funds for equipment to make the most vivid and lasting impressions and to use every art and device known to man to hold close, almost breathless, attention. How can spelling, number work, and punctuation ever hope to outrival love-making, shootings, and catching crooks? Children cannot be expected to "pay attention" or concentrate on dull school subjects when their nervous systems are overwrought, their minds unrefreshed by sound sleep, their digestion disturbed, and so forth. Rather, the conscious mind finds it is unable to stay on the track and the lurking subconscious instantly flashes a dazzling movie picture or an electrifying radio program which takes no effort whatever to follow. Is it any wonder that school standards have been lowered repeatedly and that the child's nervous system has the added strain that follows doing poor schoolwork?

Daydreaming in school by the nonaddicts was missing entirely in one-third because they kept themselves occupied, while the rest daydreamed of what they would do after school or on trips. Two preadolescent girls dreamed of handsome heroes in good movies, and two others of being singers or dancers. All their daydreams were quite uninteresting.

Another handicap to school success will be glimpsed if one considers what an inventory of the mental contents, say of average 9-year-olds, might disclose after the four, five, or six years' feasting on the weekly movies and daily radio, which consist of mysteries, adventure, war, spookies, jungle, wild west, love, gangsters, newsreels, science, comedy,

and so forth. The gourmandizing of masses of this indigestible, chaotic mixture, with no mental digestive juices powerful enough to break it up for assimilation, must lead to severe mental indigestion, if not colic or worse. Unfortunately it cannot be pumped out.

In the daydreaming of the addicts in school, again it is seen that crime execution goes over into the self committing the crime, a practice which is repeated innumerable times over the years of attendance, forming a behavior pattern that becomes deeply cut.

1. Seven-year-old: "In school I daydream of spooks and I dream of spooks, robbers and killers at night and I wake up and have to get out of bed and go to Mother."

2. Eight-year-old: "In school I can picture what I hear on the radio. In my sleep, I yell and yell."

3. Nine-year-old: "I daydream in school of 'Calling All Cars' and 'Gangbusters' and of being a king and killing all the crooks dead."

4. Ten-year-old: "In my daydreams I am the guy what does the killing by stabbing and killing enemies. The worst show I saw was where they killed lots of men and hanged them on hooks."

5. Eleven-year-old, a sissy: "I daydream I'm Nelson Eddy in the show or else I'm Jeanette McDonald."

6. Twelve-year-old: "When I'm tired of school things, I daydream of movies and the teacher hollers at me. Sometimes I'm the kid getting kidnapped."

7. Thirteen-year-old: "I can't get to bed until after ten because I have to listen to the crime with Father and in school I daydream of movie fights."

8. Fourteen-year-old, a boy: "I like love movies best and mysteries and killings next. I get most excited when they make love. In school I daydream of love movies and I pretend I'm the star."

Addiction of Unhappy Children.—It was noted with surprise that several children from well-to-do families, who were attractive but were strongly disliked by one of the parents, were almost vehement in expressing their craving for bad movies. "I love 'em; I can't see them enough times; none of them are bad enough for me," said one likeable little girl with a mother who was jealous of her. Further observation of unhappy children confirmed the impression that those most resentful of their unhappy condition were drowning their troubles in the greatest excitement they could find, and that only then could they forget their unhappiness. On the other hand, those that were utterly crushed by their rejection could not tolerate unpleasant movies for they could not stand another iota of unhappiness in any form.

A total of fifty-four unhappy children were found in the 200, of whom thirty-eight (70 per cent) revelled in the worst horrors and crime, and sixteen (30 per cent) of the more submissive were too near the breaking point to endure them.

Children who were downright happy were looked for and forty were found, all with unusual security in the home and in school and with their fellows. Of the forty, only one was a severe addict, a boy who had contracted the habit when he was very unhappy before a new, dearly loved stepmother had been acquired two years before. Seventeen had never seen a bad movie, eleven disliked them, and the rest tolerated them if they had to, the bad effects seeming somewhat neutralized by their secure status. The list of the type of movie best liked by the unhappy children ran like this for the aggressive: killings, gangsters, knife killings, murders and mysteries, spookies and shooting, where they chop them up, jungle, fighting, shooting. The submissive chose these types: love, Shirley Temple, funnies, Mickey Mouse, and children. A list of the kind best liked by happy children ran like this: funnies, old-fashioned, horses, comedy, skating, musical, mysteries that are not scary, historical, science, dancing and singing.

1. Seven-year-old: "What I like best is killings, spookies, mysteries, Tarzan, and throwing knives."

2. Eight-year-old: "Murders and gangsters are swell."

3. Nine-year-old: "I like first shooting, killings and gangsters. I saw how Lamson killed his wife but there really was not much killing in it [in a disappointed tone of voice]."

4. Ten-year-old, a timid, refined-looking girl, badly rejected: "Murders are best. Shooting and gangsters next. I liked the Vampire sucking out blood very much."

The submissive ones all said, in effect, "I just can't stand anything bad."

Love.—Love pictures and dramas were liked by fifty-three (27 per cent) and greatly disliked by most of the rest. They were admittedly liked best of all kinds by eighteen children from the ages of 10 to 16 years—six homely, fat, preadolescent girls, four potential actresses, four sissy boys in junior high school, and four adolescent girls.

It had seemed to the writer for a long time that since the advent of movies, sex awareness and sophistication concerning love matters were being awakened more and more early in the lives of children who attend. Of the fifty-three in this study who liked love pictures, twenty-four were boys and twenty-nine were girls. Five (three boys) were 8 years old; twelve (four boys) were 9 years old; eight (three boys) were 10 years old; six (four boys) were 11 years old; eight (one boy) were 12 years old; seven (four boys) were 13 years old; two girls were 14 years old; five (four boys) were 15 years old, and one boy was 16 years old. Through sympathetic participation in the experiences of the actors, these children vicariously must become familiar with the sensations aroused and undoubtedly experience bodily repercussions from the same. With much repetition, this could tend to hasten sex awareness, if not development. How weak and mild the old love novels seem by com-

parison with the ubiquitous, sensual love scenes, with their added visual and auditory appeal! A number of children, mostly boys, complained that when their mothers took them to the show, the mothers would pick out love ones because they liked them best, and while at first the children would strongly object, they would finally "get kinda used to 'em" and end by entering into the emotions portrayed. Some children learn to like the love ones in order to avoid the fearful ones while still continuing their attendance.

1. Seven-year-old, a boy: "I shut my eyes at the gangsters but love ones are nice."

2. Eight-year-old: "I like war when not too dirty and love ones if the actors are good. Mother loves to listen to the worst radio crime. I can hear from my bed but I try to think of love ones to keep the scary ones out of my mind when I'm going to sleep."

3. Nine-year-old, a girl: "I like love movies best—they are so interesting. Gangsters are shivery."

4. Ten-year-old: "I like to stay home from school and listen to the love dramas that come on in the morning."

5. Eleven-year-old: "I daydream I am at a football game and I sit near enough to my best favorite movie star so that I can watch him all the time. I cry if my best movie star dies."

6. Twelve-year-old, a sissy: "I like to think over love dramas on going to sleep and I like to dress in my sister's clothes and put on rouge and lipstick."

7. Thirteen-year-old: "I like love movies best and mysteries and killings next. I get most excited when they make love."

8. Fourteen-year-old: "I daydream of love movies and I act out the part of the star."

SUMMARY OF THE REACTIONS OF THE NONADDICTS

Of the seven who had never seen a movie, and the three who saw none until 10 to 13 years of age and then only good ones, none had sleeping or eating disturbances or bad dreams. Only one, a girl who had had a serious fright, showed nervousness. As to fears, the same girl feared a repetition of her fright. One feared kidnapping from tales heard, and one his rejecting father. None daydreamed in school of movies or radio; four did daydream of what they would do after school. On going to sleep, two sometimes thought of the mild radio programs heard; otherwise, they thought of singing, dancing, and other things they like to do.

Of the twenty-nine with a record of no bad movies or radio, outside of the cases of four spoiled children who, as usual, had sleeping, eating, and nervous disturbances, as well as fears and dreams arising from social maladjustment entailing much friction with other children, there were no fears, dreams, or sleeping or eating troubles. One-fourth were nervous over school; one child over home troubles; one boy and one girl

over severe rejection by parents; and one made nervous by an annoying, destructive, subnormal brother. Daydreaming in school was limited to the same troubles, together with two daydreaming of good movies, one spoiled boy who daydreamed of "fighting kids," and the rest daydreaming of sports, play, and what to do after school. On going to sleep, one-third thought of the mild radio program just heard; the rest of the day's doing and tomorrow's successes.

Of the two with no movies until 11 and 13 and then bad movies, and the one with good movies until 12 and then bad ones, the two boys who had lived very sheltered lives could not stand the bad ones seen, having bad dreams and fears, biting their nails at the movies, and becoming nervous afterward. The bright, well-poised 13-year-old girl soon developed an immunity after exposure and looked with a critical eye on the actors and acting.

Of the five with no movies until 10 to 13 years of age and then both bad movies and radio programs, four had built up a sufficiently stable nervous system to throw off the effects after a time, and when seen had no nervous, sleeping, or eating troubles, bad dreams or fears, although all had reacted to them at first. The fifth, a very unhappy youth waging a perpetual warfare against a perfectionistic mother, was very nervous and fearful, had eating and sleeping disturbances, and spent all spare time, when not listening to his own radio, in plotting crimes and revenge against the world.

PARENTAL ATTITUDES

As a whole, most of the foregoing reactions were not known to the parents, or if they were known, the significance was not recognized. All children were reported by parents to be in good physical condition no matter how malnourished. Nervousness was seldom reported as it was taken as a matter of course—"no more nervous than any one else" (including the parents)—and until it became annoying to the parent or school, it might be talked about (usually in the child's presence), but no cause or remedy was sought. In general, most mothers did not know how their children slept after they were small unless they themselves were disturbed, and even then night terrors and so forth were often regarded merely as a phase in development. Being thin, even scrawny, was taken as hereditary—"He has been thin for years" (and a movie and radio addict also). Not until it progressed to the stage where the school nurse fussed enough over his underweight was it given a thought. Pallor was seldom noticed, nor were habits of elimination known after the early years as a rule. Eating habits were noticed on account of the emotional charge present, which in turn prevented effective action. Other effects of movie horrors and radio crime were not even glimpsed, or, if they were, only dimly and passively.

Standards of parents could be fairly well determined by the degree of movie horrors and radio crime allowed. The same good judgment and high standards shown by restriction of attendance to once a month or less, with no horrors or radio crime, were reflected throughout the home life, regardless of social or financial status or even intelligence alone. Answers to the questionnaires showed that this type of parents did not follow the path of least resistance in anything but that they were willing to sacrifice their own convenience and unequivocably exerted great influence over their children, as evidenced by the high respect shown by the children for their parents' opinions and decisions and the desire displayed for real companionship with them, even when the discipline was strict and included physical punishment into high school age. Unless exceptional conditions supervened, these children enjoyed unusual security in their home life.

In discussion with parents of addicts, whenever opportunity allowed, the pediatrician, after eliminating organic causes, would point to concrete evidence that the health was being undermined, and in a surprising number of cases the cooperation of the parents was gained. Interference with school success was another talking point. Otherwise, the child's nagging, whining, and staging of scenes over restriction won out. "All the other kids' mothers let them go. I don't see why I can't go." But once persuaded to make a trial of eliminating bad movies and radio programs, the parents' pride in the added pounds laid on, as well as relief from the annoying disturbances, kept them to a high level of performance. It was emphasized to the parents that there were far from enough good movies produced to allow weekly attendance. Supporting measures were sought in substitutive recreation (games, trips, and so forth) and in an enlargement of the child's social life (parents' also), as well as removal of any other emotional foci of infection discovered in the examination. In these overstimulated children, one focus of infection that had to be completely excised was found to be a pocket of highly illustrated crime detective stories (infective and communicable also) sold by the chain stores for a dime each, with every other page a strikingly clear delineation of violent crime, warranted to hold even nonreading child patients from 5 years old and up, in a spellbound state. Addicts collect these "big-little" books by the dozens and by trading with each other manage to maintain a constant supply to fill any chinks in the day unoccupied by other excitement.

DISCUSSION

In view of the fact that the pediatrician is called upon more and more to do preventive work and maintain a good physical condition in his patients, this presentation is offered as a clue to further success in some of the puzzling cases that defy efforts to overcome a condition below par, no matter what physical hygiene is recommended, what carefully planned

diets are prescribed, what ideal routine is laid out, or what tonics, vitamin medication, or other measures are ordered.

Terrifying scenes can have an inhibitory effect on the functioning of every organ in the body. Eating disturbances interfere with weight gains. No child with overwrought nerves can digest his food properly; indeed, in every system, elimination, circulation, or what not, interference can take place. Bad dreams and poor sleep can cause lack of appetite, irritability, malaise, thinking difficulties, and, by reacting on the nervous system, a whole train of undesirable symptoms. In short, the patient becomes inadequate to meet life's demands without strain and shows it in his under-par condition.

A true addiction apparently develops in the devotees of "bad" movies and radio, hastened and reinforced by vicarious participation in the scenes witnessed or heard, no matter of what nature, the fascination holding even with revulsion from frightful situations. In the case of unhappy children, most of them utilize the addiction as an escape from reality, much as a chronic alcoholic does drink. The effects of habituation in the form of callousness to the suffering of others began to show as early as the seventh year and mounted year by year, leading to demands for an ever increasing dosage of ultraexciting horrors. Such an habitué is no easier to cure than any other habitué when attempting to treat the patient alone. Crime and horror were found to be uppermost in the minds of addicts much of the time day and night to the exclusion of desirable mental content, and the physical condition must pay toll for this.

Factors contributing to this condition were found to be the tendency of the mind to continue turning over throughout the night what had just been seen or heard before going to sleep—radio crime in 85 per cent of the addicts—followed by the deepening of impressions the next day by retelling and re-enacting during play time; the inability of the mind to throw off the revolting "killings" seen in movies, the shock which was experienced being repeated many times in dream life as testified by 74 per cent; the superimposition on parental kidnapping warnings to 78 per cent of addicts, of the harrowing details of film and radio scenes of sensational kidnappings; poring over the numerous illustrations of violent crime in the common "big-little" detective books; escaping dull school work by daydreaming in school of being the actor in thrilling scenes, often as the crook; and the potent tendency in the child to vicarious participation in plots seen or heard so that, in recall or dreams, he substitutes himself and family for the victim or victims, thus intensifying unwholesome emotional reactions, often to a state of fearful struggle against a terrifying threat to the safety or existence of himself and members of his family.

Most homes were found sadly lacking in resources for social and recreational outlets for either parents or children, outside of movie and radio indulgence, social prestige being gained by the degree of indulgence.

Should strong and well-enforced backing be given the movement to have suitable films shown on Saturday and Sunday afternoons when the majority of children attend, and this backing be continued after film distributors backslide as they are doing at present, benefits would accrue not only to the children but to the physicians who are called upon to keep their child patients in a good state of health. Protests in numbers to sponsors have been found effective in eliminating deleterious radio programs.

CONCLUSIONS

In a study of 200 children, addiction to movie horrors and radio crime was found to be detrimental to the general health.

Nervousness was increased both in amount (76 per cent as against 40 per cent of nonaddicts) and in degree (52 per cent extreme versus 4 per cent in controls).

Sleeping disturbances were fourfold greater in number (85 per cent versus 19 per cent), and in degree were extreme in 28 per cent versus 2 per cent.

Fears were increased fivefold (94 per cent versus 17 per cent), extreme fears being found in 42 per cent of addicts as against none in the nonaddicts.

Elimination of movie horrors and radio crime was found in homes of high standards of child training throughout, regardless of social or of economic standing, or even of intellectual standing in some cases.

Treatment, whenever possible, consisted of gaining parental cooperation by evidence that health was being undermined and school success interfered with, followed by restriction of frequency of indulgence and elimination of crime and horrors, along with substitution of other recreations and social life, which gave the satisfactory results of an improved physical condition and subsidence of symptoms.

STUDIES ON THE GROWTH AND DEVELOPMENT OF MALE CHILDREN RECEIVING EVAPORATED MILK

I. The Effect of Various Vitamin Supplements on Growth in Length and Incidence of Rickets During the First Two Years of Life

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THE acceptance and use of irradiated evaporated milk in infant feeding has become so general that it prompts an inquiry into the suitability of this food in the dietary of older children. The metabolic studies of Souders, Hunscher, Hummel, and Macy[1] indicate that there is excellent assimilation of the organic and inorganic elements of irradiated evaporated milk in young children. However, there is no body of data available concerning the growth and development of children who have received irradiated evaporated milk from infancy through the preschool years. Almost all of the studies concerning irradiated evaporated milk have been with infants for relatively short periods of observation, usually of six months' duration.

This report presents data obtained from 233 male children who have received evaporated milk as their sole source of milk since early infancy, viz., an average beginning age of 42 days. It has been the purpose of this outpatient study to observe the growth and development of these children receiving evaporated milk, to evaluate the protection against rickets afforded by the vitamin D content of the irradiated evaporated milk, and to study comparatively the influence of supplements of vitamins A, D, and B complex. The children have been in this study for periods varying from two and one-half to four years, and we are presenting data concerning selected aspects of their growth and development for a continuous two-year period of observation of each child. The majority of these children come from homes where there is financial difficulty and therefore may be considered to be representative of many children in the lower income groups of our cities. The organization of the study and methods used will be described first, and the results will then be discussed under the sections of consumption of evaporated milk, growth in length, incidence of rickets, and incidence of infections.

Subsequent reports will be made concerning the weight of these children, other anthropometric measurements, development including psychometric tests, laboratory findings, and photoelectric examination of roentgenograms of the forearm.

ORGANIZATION AND METHODS

The study was undertaken in November, 1936, in the Out-Patient Department of the Children's Hospital of Philadelphia. The personnel

From the Children's Hospital of Philadelphia.

consisted of two part-time physicians, a part-time technician, a full-time nurse and a full-time social worker. X-ray examinations were carried out in the X-ray Department of the Children's Hospital.* Infants were enrolled with the cooperation of the maternity departments of the Pennsylvania, the Philadelphia General, and the University of Pennsylvania Hospitals. Also some infants were referred from the Child Hygiene Division of the Department of Public Health of Philadelphia, others from the Children's Hospital, and a few through personal contact. The criteria set up for the selection of infants for this study were as follows:

1. All infants selected were males in order to eliminate sex as a variable.

2. All infants selected had birth weights of 5 pounds or more in order to eliminate prematurity as a factor.

3. All but four of the infants were under 3 months of age when they were enrolled. These four were under 3.5 months. The average age of the entire group was 42 days.

4. No infants were receiving any breast milk when they were referred for the study.

The last criterion eliminated so many infants that twenty-two months were required for the enrollment of the entire group.

The racial distribution of the children was 42 per cent negro and 58 per cent white. Among the white infants 25 per cent were of Italian extraction, 25 per cent of Irish, 12 per cent of British, 10 per cent of German, 7 per cent of Slavic, 11 per cent of mixed northern and southern European, and 10 per cent of mixed German and British extraction.

For the purposes of the study the 233 infants were divided into three groups according to the vitamin content of the diet they received. The colored and white infants comprising each group were considered separately in the statistical analysis. The diets were as follows:

Group I. Eighty infants received 110 U.S.P. units of vitamin D daily in the form of irradiated evaporated milk.

Group II. Seventy-three infants received approximately 1,500 U.S.P. units of vitamin D and 15,000 U. S. P. units of vitamin A daily in three teaspoons of cod-liver oil.† This group received nonirradiated evaporated milk.

Group III. Eighty infants received 110 U.S.P. units of vitamin D in the form of irradiated evaporated milk daily and 10 drops of carotene‡ (equivalent to approximately 2,250 U.S.P. units of vitamin A). A subgroup (thirty-nine infants), referred to as Group IV, received 0.5 tablespoonful of brewer's yeast powder daily (approximately 250 units of vitamin B_1 and 250 Sherman units of vitamin B_2).

*All roentgenograms were read by Dr. Ralph S. Bromer, roentgenologist of the Children's Hospital of Philadelphia.

†The cod-liver oil and yeast used in this study were made available by the generosity of Mead Johnson and Co.

‡Carotene was obtained from the S.M.A. Corporation.

All children received vitamin C in the form of orange juice or tomato juice in adequate amounts daily from the time of the first visit.

In all groups the daily formula contained one 14.5 ounce can of evaporated milk (13 fluid ounces) at or before the age of 4 months. Five per cent carbohydrate was added, usually in the form of dark corn syrup. As the children grew older, additional calories were given in solid food and the intake of evaporated milk remained the same. Banana and cereal were started at 3 to 4 months, puréed vegetables and fruits at 5 to 6 months, and potato and meat at 8 to 10 months. Egg yolk was not recommended earlier than 10 months but was given in some cases. Before the age of 1 year, the added carbohydrate was eliminated and transition from bottle to cup feeding was advised at this time. Iron ammonium citrate (18 grains daily) or a solution of ferrous sulfate (6 grains daily) was given when the hemoglobin was below 13 Gm. per 100 c.c.

In assessing the physical development of the children a definite program was followed. At the first visit the history was taken, and a complete physical examination was made. The child was weighed, and the following anthropometric measurements[2] were taken : (1) crown-heel length, (2) crown-rump length, (3) intercristal diameter, (4) width of the head, (5) length of the head, (6) circumference of the head, (7) width of the chest, (8) depth of the chest, and (9) circumference of the chest.

Clinical evidences of rickets (craniotabes, bossing, beading, Harrison's groove) were noted. A roentgenogram of the left forearm was made, and blood was taken for determination of hemoglobin and serum protein concentrations. The children were brought to the clinic at short intervals until well established on the formula and then every month during the first year, and every two months thereafter. At each regular visit the child was weighed and measured. A complete medical record was kept, including illnesses, evidence of rickets, developmental history, amount of regurgitation, and number of stools per day. Determinations of hemoglobin and serum protein were done at every second visit, and x-ray examinations of the left forearm were made ten times during the first two years, at intervals of two months from November to May and of three months during the remainder of the year.

The milk and the vitamin supplements were delivered at the homes every two weeks by the nurse and by the social worker. The number of cans of milk left was calculated so that, when the child was due for a return visit, the supply of milk was exhausted. This method was fairly effective in assuring the regularity of visits to the clinic. The supply of milk was maintained during infectious diseases and when it was temporarily impossible for the mother to bring the child to the hospital. In families where there were younger brothers and sisters, milk was supplied for them also so that there was no question of whether or not the children included in this study had had milk available. Most of the

hospitalization that was necessary was provided at the Children's Hospital where the feeding could be continued as at home.

ACCEPTABILITY OF EVAPORATED MILK AT 2 YEARS

When the children stopped drinking milk from bottles, most of the mothers put a can of milk in a quart jar and filled it up to the top with water, making a dilution of 13 fluid ounces of evaporated milk to 19 ounces of water. When the child did not finish his milk, it was recommended that 13 or 11 ounces of water should be added. In one case the milk was well taken when only 4 ounces of water were added. To obtain an approximate idea of how much milk each child was consuming, the mothers were asked from time to time if the child took a whole can daily. Although the replies to these questions may not be entirely truthful, they seemed fairly reliable and were tabulated.

TABLE I

PERCENTAGE DISTRIBUTION OF 2-YEAR-OLD CHILDREN ACCORDING TO DAILY CONSUMPTION OF EVAPORATED MILK

GROUP	RACE	NO. OF CHILDREN	1 CAN (%)	¾ CAN (%)	½ CAN (%)	¼ CAN (%)
Group I (irradiated evaporated milk)	White	48	83.3	14.6	2.1	0
	Colored	32	90.6	6.3	3.1	0
Group II (nonirradiated evaporated milk plus cod-liver oil)	White	42	90.4	2.4	4.8	2.4
	Colored	31	83.9	12.9	3.2	0
Group III (irradiated evaporated milk plus carotene)	White	24	75.0	12.5	8.3	4.2
	Colored	17	82.4	5.9	11.7	0
Group IV (irradiated evaporated milk plus carotene and yeast)	White	20	70.0	10.0	20.0	0
	Colored	19	94.7	5.3	0	0
Total	White	134	82.1	9.7	6.7	1.5
	Colored	99	87.9	8.1	4.0	0

Table I shows that the evaporated milk was well taken by the colored children and slightly less well by the white. That the carotene and yeast group of white children took less milk than the others is perhaps due to the presence of yeast in the milk; when the yeast was disliked, the best method of giving it seemed to be to sprinkle it on cereal.

GROWTH IN LENGTH

Since the children were measured at different chronological ages, at the suggestion of Dr. J. H. Austin the following method was used to determine their probable lengths at the ages which were to be tabulated. Charts were printed with a straight line representing the average rate of growth for boys from birth to 2 years, based on the average figures given by Kornfeld.[3] This line was straight instead of being the usual

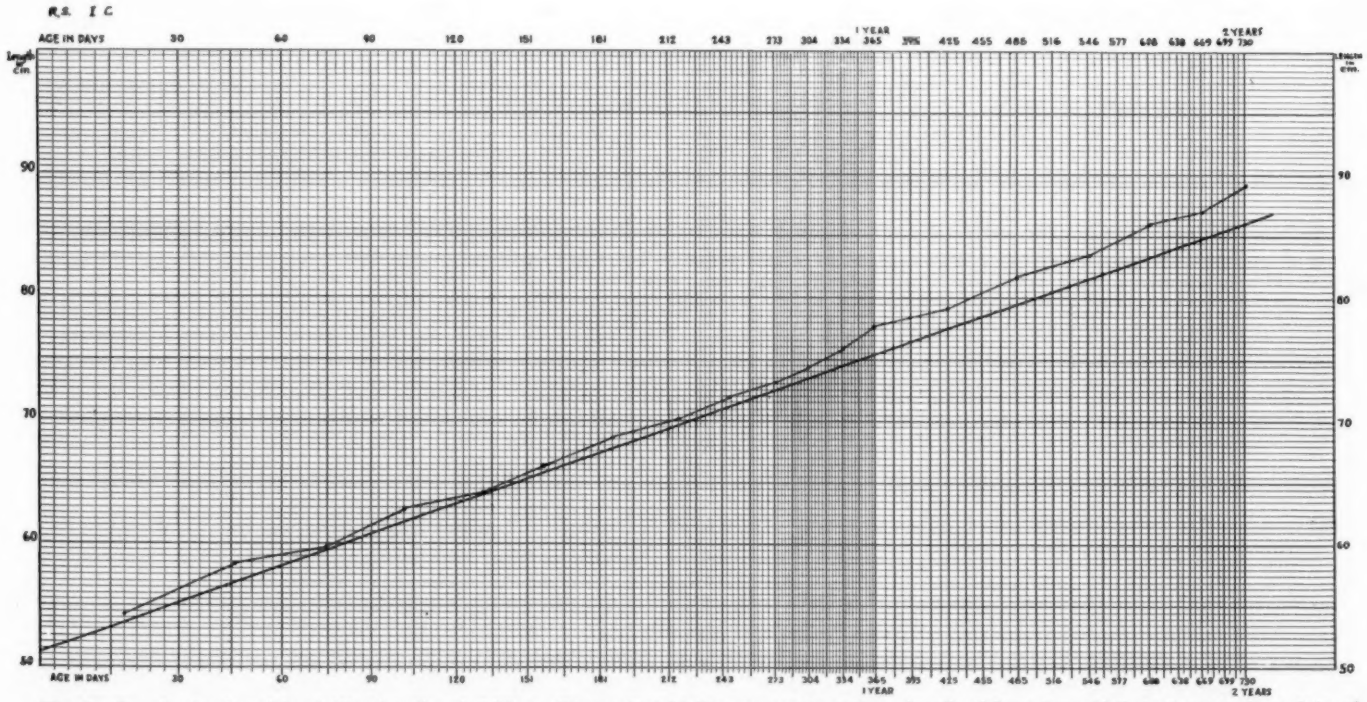
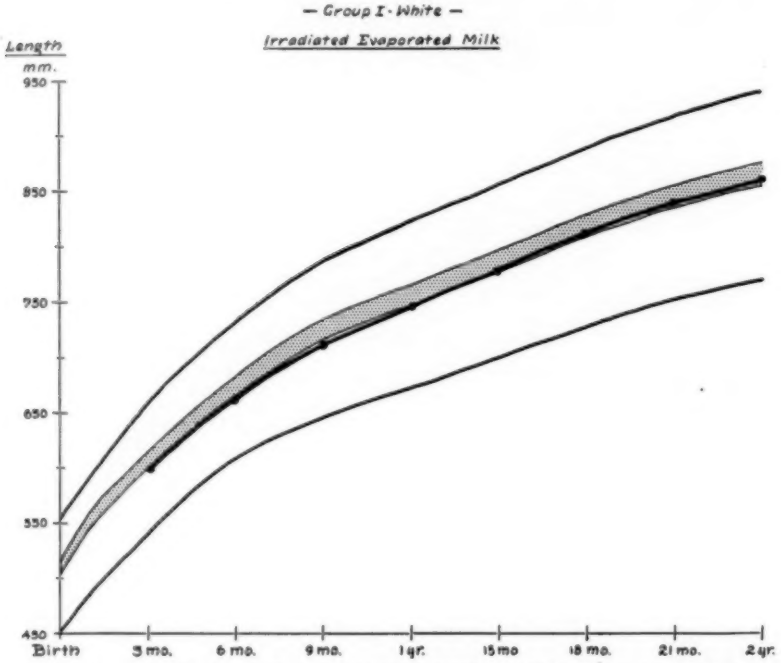


Fig. 1.—Sample chart used in plotting lengths of children. Heavy straight line represents average length of boys from birth to 2 years, from data of Kornfeld.[3] Note that ordinates representing days of age are spaced at decreasing intervals to achieve a straight line for growth in length. Measurements taken in these studies were plotted on appropriate ordinates and connected by straight lines. Length at any age between two actual measurements may be read directly from the chart.

curve because the time intervals were spaced at decreasing distances (Fig. 1). The measurements for each child and the ages in days when he had been measured were plotted on one of these charts, and the successive points were connected by straight lines. The lengths of a child at the particular ages (3, 6, 9, 12, 15, 18, 21, 24 months) were obtained directly from the intersections of the child's length line and the age ordinates. This method avoided the subjective element which enters into the interpolation of curves.



Figs. 2-9.—Growth in length compared with Kornfeld standards for boys. Stippled areas represent average range of Kornfeld standards for boys. Upper lines correspond to upper limit of height given by Kornfeld, and lower lines correspond to lower limit of length. Heavy lines are average length curves of each group.

Fig. 2.—Group I, forty-eight white children on irradiated evaporated milk.

When the growths of the children on each of the four feeding regimes were compared, the white and colored children on each diet were considered separately since it has been noted that colored children show a tendency toward more rapid growth than white children.[4] The more rapid growth of colored children was also noted in this study and warrants this division. The average lengths of the white and colored children in each of the four groups were determined at the above stated intervals and were plotted against the Kornfeld standards. These are shown in Figs. 2-9. Examination of these figures shows that the average lengths of the different groups at 3 months of age were all below

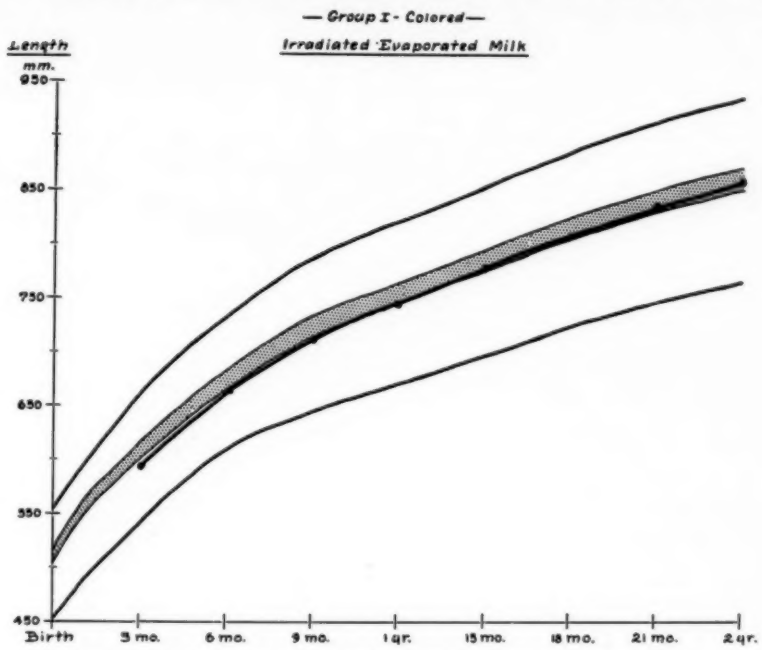


Fig. 3.—Group I, thirty-two colored children on irradiated evaporated milk.

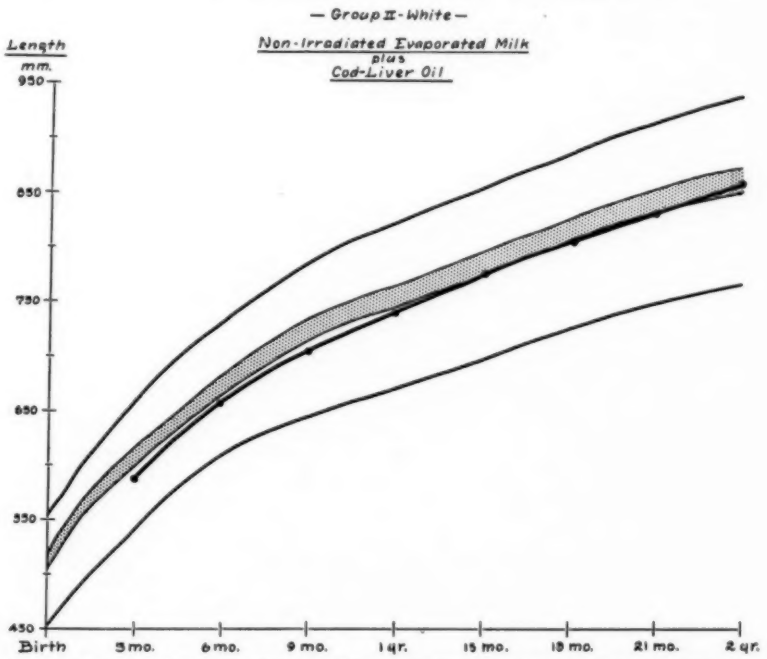


Fig. 4.—Group II, forty-two white children on nonirradiated evaporated milk plus cod-liver oil.

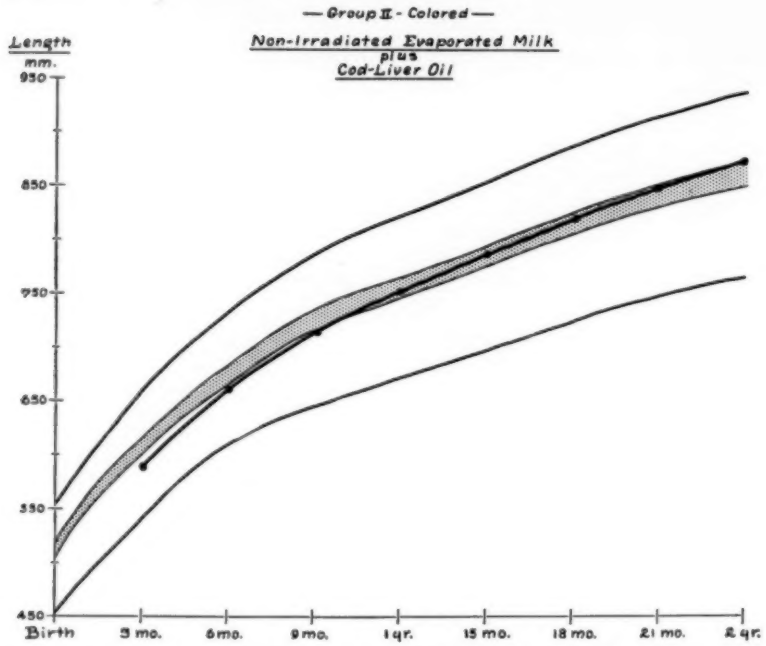


Fig. 5.—Thirty-one colored children on nonirradiated evaporated milk plus cod-liver oil.

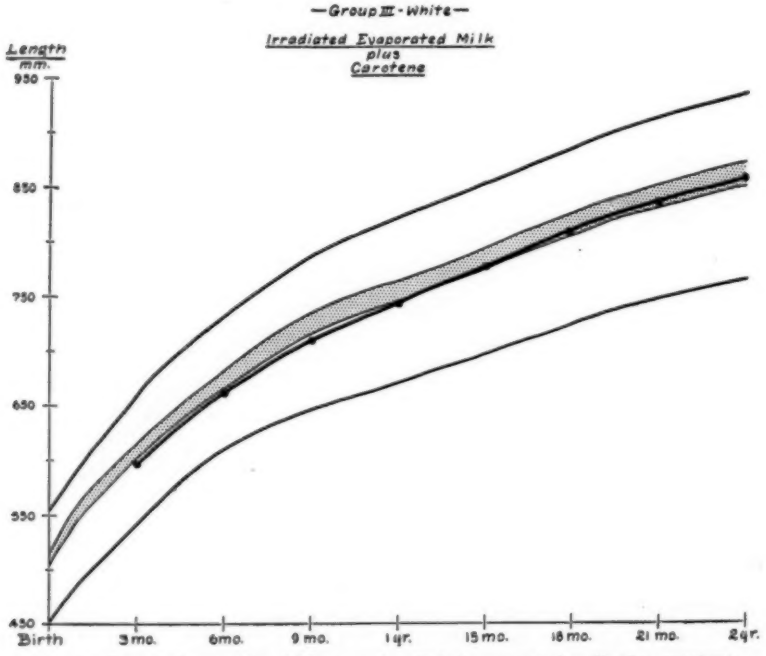


Fig. 6.—Twenty-four white children on irradiated evaporated milk plus carotene.

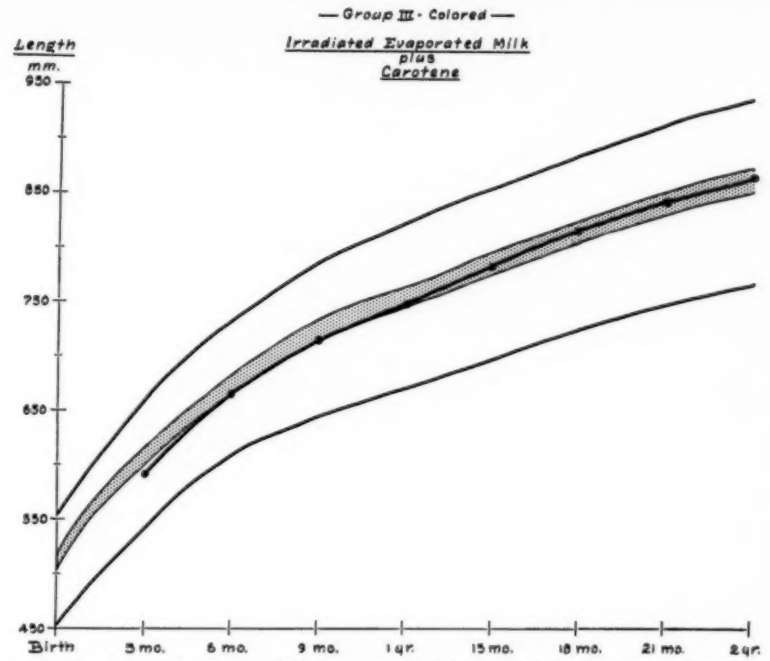


Fig. 7.—Seventeen colored children on irradiated evaporated milk plus carotene.

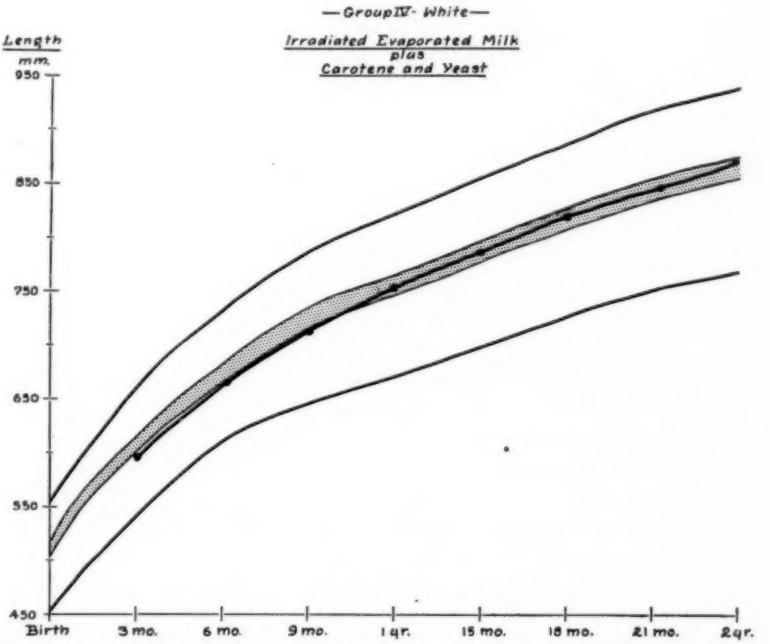


Fig. 8.—Twenty white children on irradiated evaporated milk plus carotene and yeast.

the average figures given by Kornfeld. At 2 years of age all groups had bettered their position and were within the average range of the Kornfeld standards. The Kornfeld standards correspond to those of Stuart[5] until the age of 18 months when they become definitely lower, and they are slightly lower at 1 year than those of Bakwin and Bakwin.[6] It is interesting to note that the average increment in length of the 134 white children from 3 months to 1 year was 149 mm., 1 mm. below the average increase in length of thirty-seven white children in New York, who had received fresh milk, dextrimaltose formulas plus 3 teaspoons of cod-liver oil daily from October to May and who were followed for one year by Elias and Turner.[7]

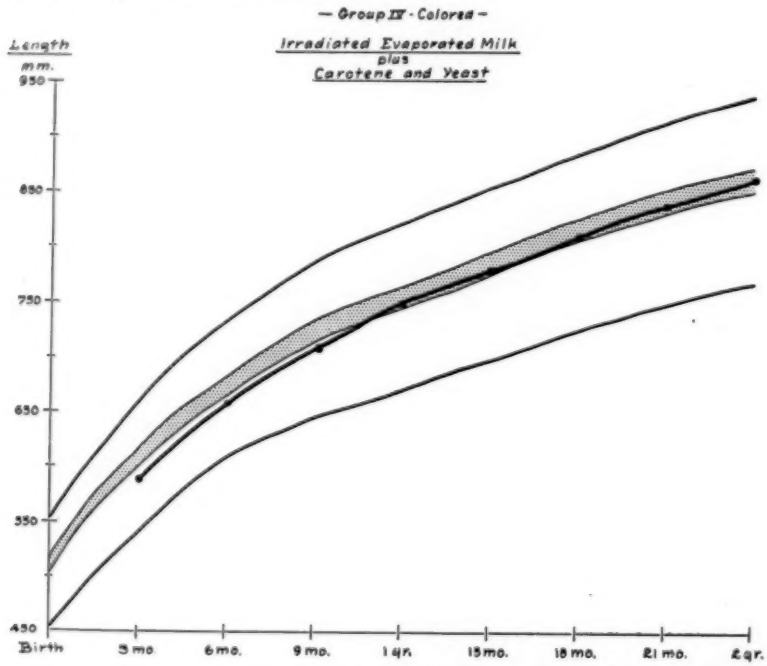


Fig. 9.—Nineteen colored children on irradiated evaporated milk plus carotene and yeast.

A summary of the average lengths at three-month intervals for the white and colored children is presented in Table II. The average lengths at 3, 12, and 24 months of both white and colored children on the four different feeding regimes were compared statistically to determine whether there were any significant differences among them. Table III summarizes the statistical data used in these comparisons. It is obvious that there was no statistical difference in the average length of either white or colored children on any of the four dietaries at 3, 12, and 24 months.

TABLE II

AVERAGE LENGTH IN MILLIMETERS ACCORDING TO AGE AND GROUP

GROUP	RACE	NO. OF CHILDREN	3 MONTHS		6 MO.	9 MO.	12 MONTHS		15 MO.	18 MO.	21 MO.	24 MONTHS	
			LENGTH (MM.)	STANDARD DEVIATION	LENGTH (MM.)	LENGTH (MM.)	LENGTH (MM.)	STANDARD DEVIATION	LENGTH (MM.)	LENGTH (MM.)	LENGTH (MM.)	LENGTH (MM.)	STANDARD DEVIATION
Group I (irradiated evaporated milk)	White	48	599	±38.1	665	710	744	±36.4	776	807	834	856	±43.8
	Colored	32	593	±44.1	664	711	745	±49.7	778	808	835	858	±54.0
Group II (nonirradiated evaporated milk plus cod-liver oil)	White	42	587	±35.8	657	704	739	±33.9	774	803	829	856	±39.8
	Colored	31	588	±52.9	660	712	750	±62.5	785	817	846	870	±77.1
Group III (irradiated evaporated milk plus carotene)	White	24	596	±42.7	661	709	743	±40.1	776	807	833	857	±52.3
	Colored	17	591	±69.1	665	713	747	±70.8	782	815	840	864	±110.0
Group IV (Irradiated evaporated milk plus carotene and yeast)	White	20	595	±61.2	665	711	751	±51.7	784	816	843	867	±75.0
	Colored	19	586	±44.2	657	706	748	±59.9	776	808	837	862	±88.8

TABLE III

COMPARISON OF LENGTHS IN MILLIMETERS OF THE DIFFERENT GROUPS AT THE AGES OF 3 MONTHS, 12 MONTHS, AND 24 MONTHS

RACE	GROUPS COMPARED	3 MONTHS			12 MONTHS			24 MONTHS		
		DIFFERENCE OF MEANS	STANDARD DEVIATION OF DIFFERENCE OF THE MEANS	SIGNIFICANCE	DIFFERENCE OF MEANS	STANDARD DEVIATION OF DIFFERENCE OF THE MEANS	SIGNIFICANCE	DIFFERENCE OF MEANS	STANDARD DEVIATION OF DIFFERENCE OF THE MEANS	SIGNIFICANCE
White	I and II	12.2	±7.9	–	4.6	±7.5	–	0.1	±8.9	–
	I and III	4.5	±10.5	–	0.9	±9.9	–	0.7	±12.6	–
	I and IV	4.4	±15.1	–	7.1	±13.0	–	10.8	±18.4	–
	II and III	8.7	±10.5	–	3.7	±9.9	–	0.8	±12.6	–
	II and IV	7.8	±15.1	–	11.7	±13.0	–	10.9	±18.3	–
	III and IV	0.9	±16.6	–	8.0	±14.5	–	10.1	±20.4	–
Colored	I and II	5.4	±12.5	–	4.6	±14.5	–	12.5	±17.1	–
	I and III	2.5	±9.6	–	2.0	±19.8	–	5.8	±29.2	–
	I and IV	7.3	±13.1	–	2.4	±16.7	–	4.4	±23.1	–
	II and III	2.9	±12.0	–	2.6	±21.1	–	6.7	±30.9	–
	II and IV	1.9	±14.2	–	2.2	±18.2	–	8.1	±25.2	–
	III and IV	4.8	±11.8	–	0.4	±22.6	–	1.4	±34.6	–

The difference in the average lengths of the two groups compared is listed in the column headed "difference of means." The standard deviation of the difference of the means was calculated from the standard deviations of the average lengths of the two groups using the formula. A significant difference between two groups is present when the difference of the means is two or more times the standard deviation of the difference of the means.

Groups I received irradiated evaporated milk; Groups II, nonirradiated evaporated milk plus cod-liver oil; Groups III, irradiated evaporated milk plus carotene; Groups IV, irradiated evaporated milk plus carotene and yeast.

The average increases in length for the white and colored children of the four groups from 3 to 24 months and their statistical attributes (namely, standard deviation of the mean and standard deviation) are tabulated in Table IV. The simple analysis of the gain in length on the four diets appeared to show significant superiority of the white children in Groups II and IV over those in Group I, and of the colored children in Group II over those in Group I. (Table IV summarizes the statistical data employed in this analysis.)

TABLE IV

SUMMARY OF STATISTICAL DATA USED IN COMPARISON OF THE INCREASES IN LENGTH BETWEEN 3 AND 24 MONTHS

	1	2	3	4	5	6
RACE	GROUP	NO. OF CHILDREN IN GROUP	MEAN INCREASE IN LENGTH (STANDARD DEVIATION OF MEAN STANDARD DEVIATION)	DIFFERENCE OF MEANS (STANDARD DEVIATION OF DIFFERENCE OF MEANS SIGNIFICANCE)		
				II	III	IV
White	I	48	*256.71* ±3.38 ±23.5	*12.19* ±5.09 Significant	*4.83* ±5.47 Not significant	*15.29* ±7.30 Significant
	II	42	*268.90* ±3.80 ±24.6		*7.36* ±5.73 Not significant	*3.10* ±7.50 Not significant
	III	24	*261.54* ±4.29 ±21.0			*10.46* ±7.76 Not significant
	IV	20	*272.00* ±6.46 ±28.9			
Colored	I	32	*264.72* ±3.36 ±19.0	*17.89* ±5.58 Significant	*8.28* ±9.39 Not significant	*11.70* ±7.82 Not significant
	II	31	*282.64* ±4.45 ±24.8		*9.61* ±9.83 Not significant	*6.19* ±8.35 Not significant
	III	17	*273.00* ±8.77 ±36.1			*3.42* ±11.29 Not significant
	IV	19	*276.42* ±7.07 ±30.8			

The mean increase in length, the standard deviation of the mean, and the standard deviation are tabulated for each group in column 3. In columns 4, 5, and 6 reading across are the differences of the means and the standard deviations of the differences of the means of the groups compared. When the difference of the means is more than twice the standard deviation of the difference of the means, the increases in length of the two groups under comparison are considered to be significantly different.

Groups I received irradiated evaporated milk; Groups II, nonirradiated evaporated milk plus cod-liver oil; Groups III, irradiated evaporated milk plus carotene; Groups IV, irradiated evaporated milk plus carotene and yeast.

However, plotting gain of length against initial length in each of the eight groups showed that in the white children of Groups I, II, and IV there was greater gain of length on the same diet when the initial length was less. This correlation was not evident in white children in Group III nor in any of the colored groups. The existence of the cor-

relation in the white children in Groups I, II, and IV suggested correcting the gain in these three groups to a common initial length. The regression coefficient from the data of these three groups pooled was Δ gain in length = 0.371 Δ initial length. Correcting the gain of these three groups by use of the regression coefficient to any arbitrary initial length reduced the difference between Groups I and II and between Groups I and IV so that the differences were no longer clearly significant. Table V summarizes the data for these corrected increases in length in Groups I, II, and IV and the values used in determining statistical differences.

While the average lengths attained at 1 and 2 years by the white or colored children in any of the four groups were not significantly different, there were some differences in the amount of growth between 3 and 24 months because of the differences in the average initial lengths at 3 months of age. Thus it is apparent that the colored children receiving 3 teaspoonfuls of cod-liver oil daily (1,500 units of vitamin D) grew significantly more than colored children receiving 110 units of vitamin

TABLE V

CORRECTED MEAN INCREASES IN LENGTH FOR WHITE CHILDREN IN GROUPS I, II, AND IV AND THEIR COMPARISON

GROUP	MEAN LENGTH AT 3 MONTHS	INCREASE FROM 3 TO 24 MONTHS CORRECTED FOR AN INITIAL LENGTH OF 594 MM.	DIFFERENCE OF MEANS (STANDARD DEVIATION OF DIFFERENCE OF MEANS)	
			2	4
I	599	258.57	*7.73*	*13.80*
		+1.86	±5.09	±7.30
II	587	266.30		*6.07*
		−2.60		±7.50
IV	595	272.37		
		+0.37		

The corrected value for the mean increase in length between the ages of 3 and 24 months was calculated in the following manner. An arbitrary initial length at 3 months of 594 mm. was taken. The difference between the actual initial mean lengths and this arbitrary mean initial length was multiplied by the regression coefficient (Δ gain in length = 0.371 Δ initial length). The value thus obtained was added or subtracted (depending on whether the actual initial mean length was greater or less than the assumed value of 594 mm.) from the actual increase in length from 3 to 24 months.

D in irradiated evaporated milk. Administration of 10 drops of carotene daily (2,250 units of vitamin A activity) to colored children receiving irradiated evaporated milk did not increase their rate of growth. Similarly daily supplements of 10 drops of carotene and 0.5 tablespoonful (5 Gm.) of powdered brewer's yeast had no added effect on the linear growth of the colored children receiving the same milk.

With the correction derived from the correlation mentioned for initial length, there were no significant differences in the amounts of growth in length from 3 to 24 months of the white children in the four groups. Although the difference was not significant, there was still a suggestive tendency for white children receiving 1,500 units of vitamin D in cod-liver oil or 110 units of vitamin D in irradiated evaporated milk plus carotene and yeast to grow more rapidly than those receiving irradiated

milk without other supplements. While the addition of vitamin A to the dietary of white children was without influence on growth in length, the administration of a supplement of B complex (yeast) had the same effect on growth in length as an increased intake of vitamin D (1,500 units).

RICKETS

For the consideration of the incidence of rickets the groups receiving irradiated evaporated milk plus carotene and those receiving irradiated evaporated milk plus carotene and yeast were combined, making groups comparable in size to those receiving irradiated evaporated milk alone and those receiving nonirradiated evaporated milk plus cod-liver oil.

TABLE VI

PERCENTAGE DISTRIBUTION OF MAXIMUM X-RAY DIAGNOSIS OF RICKETS ACCORDING TO GROUP AND RACE

GROUP	DAILY NO. OF UNITS OF VITAMIN D	RACE	NO. OF CHILDREN	NORMAL		MILD HEALED RICKETS (%)	MILD EARLY RICKETS (%)	MODERATE RICKETS (%)
				ENTIRELY NORMAL (%)	CHANGES CONSIDERED NONRACHITIC (%)			
Group I (irradiated evaporated milk)	110	White	48	35.3	43.8	8.4	12.5	0
		Colored	32	47.0	43.7	6.2	3.1	0
Group II (nonirradiated evaporated milk plus cod-liver oil)	1,500	White	42	40.4	45.2	7.2	4.8	2.4
		Colored	31	35.5	51.6	9.7	3.2	0
Group III (irradiated evaporated milk plus carotene)	110	White	44	38.6	50.0	2.3	9.1	0
		Colored	36	41.7	47.2	2.8	8.3	0

Children receiving irradiated evaporated milk and carotene are combined with those receiving irradiated evaporated milk plus carotene and yeast, to make Group III.

Roentgenographic bone changes considered nonrachitic are classified under the heading of normal.

The diagnosis of rickets was based on roentgenograms of the bones of the left forearm.[8] There is very little correlation possible between the clinical findings of rickets (craniotabes, bossing, flaring of the costal margins, beading of the costochondral junctions, and enlargement of the wrists) and the x-ray findings at the wrist.[9] The maximum amount of rachitic change found in the course of ten routine roentgenological examinations is used as the basis for the rating given to each child in Table VI.

No instance of marked rickets occurred in any group. One case of moderate rickets (0.4 per cent of the total) occurred in the group receiving nonirradiated evaporated milk and cod-liver oil. This patient was a small white child of German and Irish extraction, who grew at

an average rate. His mother, a reliable person now doing social service work, is sure that the cod-liver oil was given regularly. He was born March 29, 1937, and was first seen on April 20 when the administration of cod-liver oil was begun. At the first visit the x-ray examination was normal; at 3½ months it showed mild healing rickets and at 6 months very definite moderate healing rickets; at 8 months there was no change; and from 9 to 16 months the diagnosis was healed rickets. From 19 months on the roentgenograms have been normal.

The incidence of mild rickets in the 233 children was 13.3 per cent. Mild rickets already showing evidences of healing occurred in 6 per cent of both the white and colored groups. Mild rickets without healing was present in 7.3 per cent of the entire group (8.9 per cent of the white children and 5 per cent of the colored). The total incidence of rickets in the two groups receiving 110 units of vitamin D was 13.8 per cent as compared with 15.5 per cent in a study of ninety-seven initially nonrachitic infants receiving irradiated evaporated milk previously reported from this hospital by Rapoport, Krick, and Stokes.[9]

In Table VI it is seen that, of the children receiving irradiated evaporated milk alone, 20.9 per cent of the white and 9.3 per cent of the colored had rickets. In the cod-liver oil groups 14.4 per cent of the white and 12.9 per cent of the colored children had rickets. In the carotene groups 11.4 per cent of the white and 11.1 per cent of the colored had rickets. Findings indicate that there was no appreciable difference in the antirachitic effectiveness of 1,500 units of vitamin D in the form of cod-liver oil as compared to 110 units of vitamin D in irradiated evaporated milk.

Included in the normal groups were children whose roentgenograms showed bone changes from the normal which were not definitely rachitic. These changes consisted, for the most part, of slight cupping of the distal end of the ulna, but included slightly increased density in the zones of temporary calcification, slight decalcification, slight "spread," slight fuzziness of the distal ends of the radius and ulna, slight osteoid deposition along the inner border of the radius, etc. They occurred (Table VI) in 43.8 per cent of the white and 43.7 per cent of the colored children receiving irradiated evaporated milk, in 45.2 per cent of the white and 51.6 per cent of the colored children receiving nonirradiated evaporated milk and cod-liver oil, and in 50.0 per cent of the white and 47.2 per cent of the colored children receiving irradiated evaporated milk and carotene. The nature of these changes is not clear. Eliot and her co-workers[4] consider them as doubtful rickets, and it certainly is true that often they precede or follow an x-ray diagnosis of actual rickets. Hood and Ravitch[10] question their being rachitic, since in their study of irradiated cholesterol they found the highest percentage of these changes (37.0 per cent) in the group of white children receiving the greatest amount of vitamin D (950 to 1,200 units), while none

occurred in the colored children of that group. Jeans[11] has referred to them as "concomitants of rapid normal growth"; Robinson[12] questions this since she found them in a much smaller proportion (9.0 per cent) of the breast-fed group in her series. In this study these changes are classified as normal.

The roentgenograms of all the children were normal at 2 years with the following exceptions: three cases of slight cupping, two cases of marked, increased density of the zones of temporary calcification, and one case of marked increase in width of the zones of temporary calcification. These were all preceded by normal roentgenograms at the previous examination.

That rickets occurs more frequently in the white than in the colored[4] was borne out by this study: 15.6 per cent of the white children and 11.1 per cent of the colored having rickets. However, in the carotene group the incidence was nearly equal (11.4 per cent for the white and 11.1 per cent for the colored). In the series of children given irradiated evaporated milk studied by Rapoport, Krick, and Stokes[9] twelve of forty-seven white children developed mild rickets and three of fifty negro children developed mild rickets.

Eliot and her co-workers[4] found that the incidence of slight rickets was greater in infants who were growing rapidly than in those growing slowly when 400 units or more of vitamin D were given daily, but that this relationship was absent when the dosage was lower than 400 units. In this study no such correlation appeared when the infants were classified according to rate of growth as follows: a child was rated as growing at the average rate when his increase in length between 3 and 9 months was within 5 mm. of the average increase of his entire group for that period. When his increase in length was greater than this, he was considered to be growing faster, and, when it was less, he was considered to be growing more slowly. Table VII shows that in the cod-liver oil group rickets occurred slightly more frequently in those children who were growing at a rate slower than the average of their group. The incidence of roentgenographic bone changes not considered rachitic in this group showed almost no difference according to rate of growth. In the group receiving irradiated evaporated milk alone, the distribution of rickets and of these changes was practically the same in the fast and in the slow growing groups. In the group receiving irradiated evaporated milk plus carotene, there were somewhat more rickets and fewer questionable roentgenographic bone changes in the faster growing children.

Many studies of rickets are not continued after the infants reach the age of 6 months, and therefore some cases of rickets occur which are not reported. In this series three cases of mild healed rickets appeared at 7 to 9 months. Two of them were in the irradiated evaporated milk group; one of these was preceded by roentgenographic bone changes,

and the other was not. The third case was in the colored group receiving cod-liver oil and was preceded by the changes at only one examination.

Roentgenographic bone changes considered not rachitic occurring for the first time at 7 months or later were as follows: irradiated evaporated milk group, white 10.4 per cent, colored 9.4 per cent; cod-liver oil group, white 19.0 per cent, colored 22.6 per cent; irradiated evaporated milk plus carotene, white 13.6 per cent, colored 5.6 per cent. No conclusions are drawn from the fact that the greater percentage of delayed changes occurred in the groups receiving the larger amount of vitamin D.

TABLE VII

INCIDENCE OF RICKETS ACCORDING TO GROUP AND RATE OF GROWTH BETWEEN 3 AND 9 MONTHS

GROUP	RACE	RATE OF GROWTH	NO. OF CHILDREN	NORMAL	CHANGES CONSIDERED NONRACHITIC	EARLY MILD RICKETS	EARLY HEALED RICKETS	MODERATE RICKETS
Group I (irradiated evaporated milk)	White	Faster	16	5	8	2	1	
		Av.	15	4	7	2	2	
		Slower	17	8	6	2	1	
	Colored	Faster	11	5	5		1	
		Av.	9	5	3		1.	
		Slower	12	5	6	1		
Group II (nonirradiated evaporated milk plus cod-liver oil)	White	Faster	13	6	5		2	
		Av.	15	4	10			1
		Slower	14	6	5	2	1	
	Colored	Faster	13	4	8		1	
		Av.	8	3	3		2	
		Slower	10	3	6	1		
Group III (irradiated evaporated milk plus carotene)	White	Faster	14	6	5	2	1	
		Av.	16	8	8			
		Slower	14	3	9	2		
	Colored	Faster	14	6	6	2		
		Av.	7	1	5	1		
		Slower	15	8	6	1		

A child was classified as growing at the average rate when his increase in length between 3 and 9 months was within 5 mm. of the average increase of his entire group. When the increase was greater, he was rated as growing faster; and, when it was less, he was rated as growing more slowly.

The total incidence of rickets in this series was 13.7 per cent, rather lower than that found in many studies. Eliot and her co-workers,[4] in Detroit, using 135 units to 735 units of vitamin D in various antirachitic agents, found rickets, exclusive of doubtful rickets (corresponding to those in this study reported as roentgenographic bone changes considered nonrachitic) in 36 per cent of white males and 28 per cent of colored males. Robinson[12] found the incidence of definite rickets to be 33 per cent in St. Louis. Roddy and his co-workers,[13] in Philadelphia, found 25 per cent rickets occurring in eighty-four initially nonrachitic infants followed for four and a half months on 2,140 or 1,070 units of vitamin D in the form of percomorph-liver oil. Other studies find lower

TABLE VIII

NUMBER OF INFECTIONS PER CHILD FROM 3 TO 24 MONTHS ACCORDING TO GROUP

GROUP	RACE	NO. OF CHILDREN	COLDS			OTITIS MEDIA	PNEUMONIA	SPECIFIC INFECTIONS	CERVICAL LYMPHADENITIS	ECZEMA	DIARRHEA	
			MILD	MODERATE	SEVERE						WITH PARENTERAL INFECTION	WITHOUT PARENTERAL INFECTION
Group I (irradiated evaporated milk)	White	48	4.42	0.73	0.44	0.35	0.06	0.47	0.02	0.04	0.17	0.25
	Colored	32	6.19	1.0	0.44	0.28	0.03	0.38	0.03	0.13	0.28	0.34
Group II (nonirradiated evaporated milk plus cod-liver oil)	White	42	4.10	0.62	0.60	0.33	0.07	0.14	0.0	0.10	0.14	0.26
	Colored	31	5.32	0.77	0.58	0.35	0.07	0.42	0.0	0.07	0.29	0.42
Group III (irradiated evaporated milk plus carotene)	White	24	4.25	1.25	0.79	0.29	0.08	0.33	0.13	0.08	0.66	0.17
	Colored	17	5.12	0.76	0.59	0.24	0.0	0.24	0.06	0.24	0.35	0.35
Group IV (irradiated evaporated milk plus carotene and yeast)	White	20	4.95	1.50	0.50	0.40	0.05	0.05	0.0	0.10	0.20	0.40
	Colored	19	6.05	0.84	0.53	0.32	0.0	0.21	0.11	0.11	0.05	0.47

incidences of rickets, but it seems to be true that a certain amount of clinically insignificant rickets is bound to occur with usual doses of customary antirachitic agents, and in this study irradiated evaporated milk has been essentially as efficacious as large amounts of cod-liver oil.

INCIDENCE OF INFECTIONS

In Table VIII the incidence of infections is reported according to the number of infections occurring in each group per child in that group. It will be noticed that there were more mild colds among the colored children than among the white. Diarrhea without parenteral infection was slightly more frequent in the groups receiving yeast. The white group receiving irradiated evaporated milk plus carotene had more severe colds, slightly less otitis media, and more diarrhea with parenteral infection and less without parenteral infection. Obviously carotene had no beneficial influence on the number or severity of respiratory tract or other infections.

There were four cases of lipoid pneumonia which are not included in Table VIII. One occurred in a colored child receiving irradiated evaporated milk; it was learned that he had received cod-liver oil for ten days early in infancy. Two occurred in the cod-liver oil group, one white and one colored. The fourth case occurred in a white child receiving carotene. All have done well except the colored one who received cod-liver oil and who has remained small and thin with poor musculature.

In general, there was little difference between the groups in the incidence of infections.

CONCLUSIONS

Longitudinal observation has been made of 233 male infants receiving diets containing evaporated milk as the sole source of milk from an average initial age of 6 weeks until the age of 2 years. The acceptability of evaporated milk by children beyond the period of infancy was noted.

The infants were divided into four groups according to vitamin supplements. Group I received irradiated evaporated milk; Group II, nonirradiated evaporated milk plus cod-liver oil; Group III, irradiated evaporated milk plus carotene; Group IV, irradiated evaporated milk plus carotene and yeast.

The average growth in length of all groups was better than would have been expected according to the Kornfeld standards of normal growth of boys, and there was no significant difference in length between any of the groups at 3 months, 1 year, or 2 years.

White children receiving 1,500 units of vitamin D in the form of cod-liver oil between the ages of 3 months and 2 years, increased in length by a suggestively, although not clearly significantly, greater amount than the children receiving 110 units of vitamin D in irradiated

evaporated milk without added vitamins A and B. Colored children receiving cod-liver oil increased in length a significantly greater amount than those receiving irradiated evaporated milk.

Addition of 2,250 units of vitamin A in the form of carotene produced no significant effect on rate of growth in length of either the white or colored children.

White children receiving carotene and approximately 250 units of vitamins B_1 and B_2 in powdered brewer's yeast between the ages of 3 and 24 months increased in length by a suggestively, although not clearly significantly, greater amount than the children on the same milk not receiving these vitamin supplements. For the colored children, addition of yeast produced no significant increase in length.

The incidence of roentgenographic rickets was practically the same at both levels of vitamin D intake (110 and 1,500 units daily).

The various vitamin supplements had no influence on the incidence or severity of infections of the upper respiratory tract.

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INTAKE OF AMINO ACIDS BY BREAST-MILK-FED INFANTS AND AMINO ACID COMPOSITION OF COW'S MILK AND HUMAN MILK

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IN THE past the nitrogen requirement of man has been concerned primarily with protein requirement, but with advancing knowledge of the composition and nutritive behavior of the different proteins, it has become evident that the nutritive value of a protein resides in its component parts, the individual amino acids. Proteins contain twenty or more amino acids; the variety of proteins in body tissues and fluids are composed of numerous combinations of these amino acids, varying in number and quantity. Some of the amino acids can be synthesized by the body; others must be furnished directly in the food pabulum. The amino acids which cannot be synthesized by the body and are necessary for growth or maintenance are known as "essential amino acids."

Our concept of the nutritional significance of amino acids, the digestion products of proteins, is based upon such classic investigations as those of Osborne and Mendel[1, 2] and Rose.[3] Workers in the field of amino acid requirement have derived their conclusions from studies of the growth of the white rat. At the present time it is clear that lysine, tryptophane, histidine, phenylalanine, leucine, isoleucine, threonine, methionine, and valine are essential to the growth of rats consuming an otherwise adequate diet, for omission of any one of these amino acids from the diet results in cessation of growth.

Arginine occupies an interesting position among the amino acids. Growth will occur at a subnormal rate in its absence, but arginine must be present for normal growth to take place.[3] Cystine is also of considerable significance. While cystine is not essential in the diet of the rat to produce growth, its presence reduces to some extent the requirement for methionine. This fact illustrates the synergistic relationship which exists between the amino acids which are not absolute essentials and those which are indispensable for growth.

Amino acid intake is important to the organism not only for the support of growth but also for body maintenance or replacement of endogenous losses. Recent work by Burroughs, Burroughs, and Mitchell[4] has shown that amino acid requirements for growth and maintenance differ. The growth essentials, lysine, leucine, histidine, arginine, and phenylalanine, are not required for maintenance of the adult rat.

From the Research Laboratory of the Children's Fund of Michigan, Detroit.

Methionine, which will fulfill both cystine and methionine requirements, is an essential for the adult animal. These investigators have been able to maintain animals in nitrogen equilibrium with a mixture of threonine, isoleucine, tryptophane, valine, methionine, tyrosine, and norleucine as the sole source of nitrogen. Furthermore, they have shown that 30 to 50 per cent of the body maintenance requirement for nitrogen in their animals could be satisfied by a variety of incomplete amino acid mixtures, thus demonstrating that some of the nitrogen requirement does not demand specific amino acid structures.

Studies with white rats indicate, in general, the significance of specific amino acids in the maintenance and growth of all animals. However, the conclusions derived cannot be applied directly to nutrition problems in man. Little information is available in the literature concerning amino acid requirement and daily intake at any age by human subjects.

The application of newer and more satisfactory methods of determining individual, nutritionally essential amino acids has provided more accurate estimation of the constitution of the proteins of human milk and cow's milk. The basic amino acid composition of cow's milk casein, has been established by Vickery and White,[5] using the macromethod. These data have been extended in a recent publication from this laboratory[6] to cover seven amino acids in both the casein and soluble protein fractions of both human milk and cow's milk.

In view of the fact that in the literature there is no information on the quantitative nitrogen requirement of man as it pertains to the amino acids, it has been helpful to us and it seems justifiable to present an estimate of infants' consumption of certain amino acids and the records of the infants' concurrent growth and development. We have estimated the intake of seven amino acids by three infant girls whose sole source of dietary nitrogen during their first six months of life was their respective mothers' milk.

The infants studied had healthy nutritional histories, judging from detailed physical, medical, and x-ray examinations of both mother and child. Breast milk and water were the only foods received by the infants during the period studied. Milk was expressed at four-hour intervals and pooled in twenty-four-hour samples by each mother, all of whom were experienced in the technique of manual expression of milk. A portion of the pooled milk was taken for total and nonprotein nitrogen determinations, and the rest was stored for bottle feeding the following day. In accordance with pediatric practice, the milk was fed at four-hour intervals, but the record presents the amount of milk voluntarily selected by the children. The growth rate of each child, average daily milk volume consumption, and the average daily nitrogen intake were determined.

Infants A and B were studied continuously from birth through the fifth month of life, while Infant C was studied only in her fourth and fifth months. Infants A and B weighed 3.84 and 3.91 kg., respectively, at birth and made nearly equal weight gains throughout the study. Furthermore, they consumed approximately equal volumes of milk which, however, differed each month in protein content. Infant C, who weighed 3.06 kg. at birth, was growing at a satisfactory rate but was 1 kg. smaller than the others during her fourth and fifth months of life. She had a correspondingly low milk volume intake, but, since her mother's milk was of a considerably higher nitrogen content per unit volume, her level of protein intake was essentially the same as that of Infants A and B, and her weight gain was equal to that of the larger children.

Infants A and B, respectively, gained 3,260 and 3,220 Gm. of body weight during their first five months of life while consuming totals of 116.5 and 115.2 liters of their mothers' milk, containing 1,114 and 1,209 Gm. of protein. Using Rubner's estimate of 30 Gm. of nitrogen per kilogram of body tissue, the gains of 3.26 and 3.22 kg. by the infants indicate a storage of approximately 611 and 604 Gm. of protein in the body tissues. Infant C gained 1,020 Gm. of body weight during her fourth and fifth months of life while ingesting 40.7 liters of her mother's milk, containing 518 Gm. of protein. By Rubner's calculation the gain of slightly more than 1 kg. indicates a storage of 191 Gm. of protein in body tissue.

The adaptability of human breast milk to the requirements of the infant body is strikingly illustrated by the weight gains and nitrogen deposition of the three infants. If we determine by Rubner's factor the monthly deposition of protein in body tissue per kilogram of body weight, and if from the protein nitrogen intakes we estimate the protein intakes per kilogram of body weight, the monthly protein intake, deposition, and milk volume intake by the three infants can be compared.

Table I shows gradual decreases in volume intake of breast milk per kilogram of body weight accompanied by decreasing protein intakes on the unit weight basis; however, the estimated deposition of protein in body tissue was much higher during the second and third months than in the first month of life but dropped below the first month level during the fourth and fifth months. The values for Infant C, studied in only her fourth and fifth months, conformed with those of the other two girls at the same age, although they were slightly higher than those for Infants A and B, perhaps owing to compensation for her lower birth weight.

During their first three months of life, Infants A and B made average monthly gains in body weight amounting to 159 and 150 Gm., respectively, per kilogram of body weight. During their fourth and fifth months of life, the corresponding gains in body weight were 68 and

76 Gm., respectively. The demand per kilogram of body weight for protein for the construction of tissue was reduced after the first three months, and the rate of weight gain decreased. The total weight gains, breast milk and protein intakes, and estimated deposition for the three infants during their fourth and fifth months of life are presented in Table II.

TABLE I

BREAST MILK AND PROTEIN INTAKES AND ESTIMATED PROTEIN DEPOSITION OF THREE INFANTS PER KILOGRAM OF BODY WEIGHT PER MONTH

INFANT	AGE (MO.)	INTAKE		ESTIMATED PROTEIN DEPOSITION*	
		MILK (LITERS)	PROTEIN (GM.)	GR.	% INTAKE
A	1	4.5	68.4	34.1	50
B	1	4.5	54.4	26.6	49
A	2	4.4	32.2	25.7	80
B	2	4.4	47.2	31.3	66
A	3	4.3	43.1	29.6	69
B	3	4.3	37.7	26.2	69
A	4	3.8	31.3	13.1	42
B	4	3.8	44.2	13.5	30
C	4	4.0	49.9	20.1	40
A	5	3.8	31.7	12.4	39
B	5	3.8	36.6	14.8	40
C	5	3.3	42.9	14.4	34

*Based on Rubner's estimate of 30 Gm. of nitrogen per kilogram of body tissue.

TABLE II

TOTAL WEIGHT GAINS, BREAST MILK AND PROTEIN INTAKES, AND ESTIMATED PROTEIN DEPOSITION FOR THREE INFANTS DURING THEIR FOURTH AND FIFTH MONTHS OF LIFE

	INFANT		
	A	B	C
Gain in body weight (Gm.)	900.00	1,000.00	1,020.00
Breast milk intake (liters)	50.50	50.10	40.60
Protein concentration/liter (Gm.)	8.28	10.62	12.76
Protein intake (Gm.)	418.00	532.00	518.00
Estimated protein deposition:*			
Grams	169.00	188.00	191.00
Per cent intake	40.40	35.30	36.90

*Based on Rubner's factor of 30 Gm. nitrogen per kilogram of body weight.

INTAKE OF SEVEN AMINO ACIDS FROM BREAST MILK BY THREE INFANTS

The present estimation of the approximate amino acid consumption of healthy growing infants constitutes one of the first attempts to determine specific amino acid intake of human subjects. Investigation of amino acid ingestion and growth is of special interest in view of recent studies on oral and intravenous administration[7] and therapeutic use[8, 9] of casein hydrolysates and other amino acid mixtures.

From the nitrogen content of the infants' milk consumption, 36 mg. per 100 ml. of breast milk were deducted for nonprotein nitrogen, and

TABLE III

AVERAGE NITROGEN DISTRIBUTION IN MILK
(Mg./100 Ml.)

	COW'S MILK	HUMAN MILK
Number of samples	3	4
Total nitrogen	517.6	161.6
Casein nitrogen	404.6	48.6
Whey protein nitrogen	88.8	77.0
Nonprotein nitrogen	24.2	36.0

the remaining nitrogen was distributed between casein and whey protein fractions in the proportions determined for mature human milk (Table III). Early lactation includes the colostral and transitional periods of milk secretion, in which the nitrogen fractions are known to be higher[10] and of somewhat different distribution. Inasmuch as the mothers were multiparas and established mature milk flow very early in lactation, the application of our present analytical values to the first and second months of infant feeding (Infants A and B) is of interest. From the data on the growth of the infants and their quantitative consumption of breast milk of known nitrogen content, and from the analytical data on the amino acid composition of breast milk proteins,[6] the average daily intakes of seven amino acids were estimated and are presented in Table IV for each month of study.

During their second through fifth months of life, Infants A and B received from their mothers' milk protein which furnished, respectively, approximately 13 and 15 Gm. histidine, 42 and 50 Gm. arginine, 52 and 62 Gm. lysine, 52 and 62 Gm. tyrosine, 20 and 23 Gm. tryptophane, 21 and 25 Gm. cystine, and 19 and 23 Gm. methionine. Although it is difficult, if not impossible, to assess accurately the physiologic value of milk proteins for growth without considering the function of maintenance, the efficiency with which the infants must have utilized milk protein in increasing their body size should be noted. If Infant A, for example, had used 825 Gm. of dietary protein in producing 467 Gm. of body protein, or 2,490 Gm. of human flesh, it is important to learn what happened to the remaining 358 Gm. of protein taken into the body and what was the preferential selection ratio of the various amino acids by the body in its physiologic synthesis of tissue proteins. Did this excess serve as a factor of safety in growth or did some of it actually enter into the function of maintenance of the other 5 kg. of living body tissue? Growth cannot occur unless a very definite minimum assortment of essential amino acids is available to satisfy the current needs of the cells.

Table V shows the infants' intakes of the seven animo acids in milligrams per kilogram of body weight per day. Omitting the first month of life, it is evident that while there was variability from month to month, the general tendency was to maintain some degree of constancy

TABLE IV

DAILY NITROGEN AND ESTIMATED AMINO ACID INTAKE, IN THE FORM OF BREAST MILK PROTEIN, BY THREE HEALTHY INFANT GIRLS DURING THEIR FIRST FIVE MONTHS OF POSTNATAL LIFE

	FIRST MONTH‡		SECOND MONTH		THIRD MONTH		FOURTH MONTH			FIFTH MONTH		
	INFANT A	INFANT B	INFANT A	INFANT B	INFANT A	INFANT B	INFANT A	INFANT B	INFANT C	INFANT A	INFANT B	INFANT C
Average body weight (kg.)*	4.22	4.21	4.95	4.92	5.75	5.73	6.42	6.36	5.33	6.87	6.86	5.84
Gain in weight (kg.)†	0.77	0.60	0.68	0.82	0.91	0.80	0.45	0.46	0.57	0.45	0.54	0.45
Average daily intake:												
Breast milk (ml.)	639	630	735	725	825	813	822	813	704	862	858	651
Protein nitrogen (gm.)	1.54	1.22	0.85	1.24	1.32	1.15	1.07	1.50	1.42	1.16	1.34	1.34
Histidine (mg.)	151	119	83	122	130	112	105	147	139	114	131	131
Arginine (mg.)	491	388	271	398	421	366	341	477	453	370	427	427
Lysine (mg.)	609	481	336	493	522	454	423	592	563	459	530	530
Tyrosine (mg.)	607	478	335	491	520	451	421	589	560	457	527	527
Tryptophane (mg.)	229	181	126	186	197	171	159	223	212	173	200	200
Cystine (mg.)	241	191	133	196	208	180	169	235	223	182	210	210
Methionine (mg.)	223	176	123	180	191	166	154	216	205	167	194	194
Cystine-S + methionine-S (mg.)	112	89	62	91	96	84	78	109	104	85	98	98

*Birth weights: A, 3.84 kg.; B, 3.91 kg.; C, 3.06 kg.

†Gain in weight from the first to the last day of the month.

‡The application of our analytical data upon the amino acid content of mature human milk in the calculation of the amino acid intakes during the first month, which includes the colostral and transitional periods of secretion, may have introduced some deviation from the true values.

TABLE V

DAILY NITROGEN AND ESTIMATED AMINO ACID INTAKE PER KILOGRAM OF BODY WEIGHT IN THE FORM OF BREAST MILK PROTEIN BY THREE INFANT GIRLS DURING THEIR FIRST FIVE MONTHS OF POSTNATAL LIFE

	FIRST MONTH*		SECOND MONTH		THIRD MONTH		FOURTH MONTH			FIFTH MONTH		
	INFANT A	INFANT B	INFANT A	INFANT B	INFANT A	INFANT B	INFANT A	INFANT B	INFANT C	INFANT A	INFANT B	INFANT C
Average body weight (kg.)	4.22	4.21	4.95	4.92	5.75	5.73	6.42	6.36	5.33	6.87	6.86	5.84
Gain in weight (Gm./kg.)	182	142	137	167	158	140	70	72	107	66	79	77
Average daily intake (mg./kg. body weight):												
Protein nitrogen	365	290	172	252	230	201	167	236	266	169	195	229
Histidine	36	28	17	25	23	20	16	23	26	17	19	22
Arginine	116	92	55	81	73	64	53	75	85	54	62	73
Lysine	144	114	68	100	91	79	66	93	106	67	77	91
Tyrosine	144	114	68	100	91	79	66	93	105	66	77	90
Tryptophane	54	43	26	38	34	30	25	35	40	25	29	34
Cystine	57	45	27	40	36	31	26	37	42	26	31	36
Methionine	53	42	25	37	33	29	24	34	38	24	28	33
Cystine-S + methionine-S	27	21	12	18	17	15	12	17	19	12	14	17

*The application of our analytical data upon the amino acid content of mature human milk in the calculation of the amino acid intakes during the first month, which includes the colostral and transitional periods of secretion, may have introduced some deviation from the true values.

in intake per kilogram, largely owing to the increasing milk consumption of the growing infants to cover their constantly expanding caloric requirement. The extremes of variation in amino acid intake by the three healthy infants were: histidine, 16 to 26 mg.; arginine, 53 to 85 mg.; lysine, 66 to 106 mg.; tyrosine, 66 to 105 mg.; tryptophane, 25 to 40 mg.; cystine, 26 to 42 mg.; and methionine, 24 to 38 milligrams per kilogram of body weight per day.

While growth of an organism may be limited primarily by the supply of any single growth essential, whether it be mineral element, essential fatty acid, vitamin, or essential amino acid, it is ultimately limited under conditions of optimal supply of nutrients by the individual's inherent physiologic capacity for growth. Whether under conditions of greater protein supply the infants in the present study would have grown at more rapid rates than shown in their excellent records is a matter of speculation. It is evident that the protein in the mothers' milk did not furnish a liberal surplus of amino acids over the amounts laid down in tissue, but it is known that with respect to protein as well as energy the body is more efficient in its utilization at low than at high levels of intake. However, only with a protein of nearly ideal amino acid composition pattern could one expect to find such efficient utilization.

RELATIONSHIP AMONG AMINO ACID COMPOSITIONS OF HUMAN MILK, COW'S MILK, AND MODIFIED COW'S MILK USED IN INFANT FEEDING

Clinical studies[11, 12] have demonstrated that human milk has nutritive advantages over other types of infant food, although in which of the nutrient phases the superiority resides has never been clear. The advantageous properties have been sought in the components of the ash, the vitamins, and the protein mixtures.

In spite of the differences in distribution of protein nitrogen between casein and whey protein (Table III) in human milks and cow's milk, "there is a surprising similarity in contour of the amino acid composition of the protein mixtures with respect to histidine, arginine, lysine, tyrosine, and tryptophane. . . . The similarity in composition of the milk protein mixtures of the two species is not carried out with respect to cystine and methionine, although the amounts of sulfur furnished by the proteins of the two milks are approximately equivalent."[6] These facts become evident by comparing the amino acid composition of 100 ml. of human milk with that of an equivalent amount of cow's milk protein (Table VI).

Both cystine and methionine are constituents of tissue protein and therefore are required for the deposition of tissue in the growing organism. If methionine can replace cystine in the diet of the growing infant, it would appear that as far as composition with respect to seven of the amino acids is concerned, there would be little nutritive advantage of

TABLE VI

AMINO ACID COMPOSITION OF THE TOTAL PROTEIN IN HUMAN MILK AND IN COW'S MILK

	HUMAN MILK	COW'S MILK	
	MG./100 ML.	MG./100 ML.	MG./25.5 ML.*
Nitrogen	125.6	493.4	125.6
Histidine	12.3	59.3	15.1
Arginine	40.0	127.3	32.4
Lysine	49.7	222.6	56.7
Tyrosine	49.6	197.3	50.2
Tryptophane	18.7	42.6	10.8
Cystine	19.8	22.8	5.8
Methionine	18.1	103.7	26.4
Cystine-S	5.3	6.0	1.5
Methionine-S	3.8	22.3	5.7
Cystine-S + methionine-S	9.1	28.3	7.2

*25.5 ml. of cow's milk contains a quantity of protein nitrogen equal to that in 100 ml. of human milk.

one type of protein over the other. While the ability of methionine to replace cystine in the diet of the growing rat has been amply demonstrated, the ability of the human infant to make the conversion is still unproved. If such a conversion were difficult or occurred only to a limited extent, the biologic value of human milk protein for the infant might be greater than that of an equal quantity of cow's milk protein. If the cystine requirement of the infant is high, cow's milk protein must be fed in larger amounts than human milk protein to satisfy this cystine requirement; otherwise the conversion of some methionine to cystine would have to be performed by the infant.

This difference between cow's milk and human milk in distribution of sulfur between cystine and methionine is of special significance in view of recent research on the nutritive value of milks. Blazso[13] has obtained evidence that breast milk is superior to cow's milk in promoting sulfur retention in the human infant. Ujsaghy[14] has found a higher ratio of sulfur to nitrogen retention in infants consuming breast milk than in infants consuming cow's milk. The nutritive superiority of one type of milk protein over another would appear to be not so closely related to the amount of sulfur present in the protein or to the ratio of sulfur to nitrogen in the protein, but rather, fundamentally, to be connected with the distribution of sulfur and nitrogen among the nutritionally essential amino acids.

Inasmuch as cow's milk and human milk contain an equal number of calories per unit volume, unmodified cow's milk fed to an infant would furnish considerably more protein nitrogen than an isocaloric quantity of human milk. It would be equally as satisfactory as human milk in furnishing histidine, arginine, lysine, tyrosine, tryptophane, cystine, and methionine; in fact, it would furnish a higher surplus of all but cystine. Such a surplus of amino acids would allow a greater factor of safety in nutrition but only at the expense of considerably increasing

the protein metabolism of the child, a procedure which might or might not be uniformly satisfactory.

SUMMARY

Records of three infant girls' growth and nitrogen intake from their respective mothers' milk provide data upon the relationships between gain in body weight, volume intake of milk, concentration of protein in human milk, and estimated protein deposition in body tissue.

The amino acid intakes from breast milk protein by two normal, healthy infant girls during the first five months of life and for a third infant girl during her fourth and fifth months of life have been estimated from amino acid analyses of human milk proteins. During their first five months, two infants of similar birth weight gained 3,260 and 3,220 Gm. of body weight, respectively, from 116.5 and 115.2 liters of their mothers' breast milk, containing 1,114 and 1,209 Gm. of protein. By Rubner's estimate of 30 Gm. of nitrogen per kilogram of body tissue, 611 and 604 Gm. of protein, respectively, were deposited in the infants' bodies, or approximately one-half of the protein intake. The third infant, who weighed approximately 800 Gm. less at birth, demonstrated equally satisfactory gains in body weight on less milk of greater protein concentration.

Calculated from analyses of mature human milk, these two infants' intakes of seven amino acids during their second through fifth months of life were, respectively, 13 and 15 Gm. histidine, 42 and 50 Gm. arginine, 52 and 62 Gm. lysine, 52 and 62 Gm. tyrosine, 20 and 23 Gm. tryptophane, 21 and 25 Gm. cystine, and 19 and 23 Gm. methionine.

A comparison has been made of the composition of cow's milk and human milk proteins with respect to seven amino acids, histidine, arginine, lysine, tyrosine, tryptophane, cystine, and methionine. Gram for gram of protein, the two milks are nearly equivalent in histidine, arginine, lysine, tyrosine, tryptophane, and organic sulfur; however, the organic sulfur in human milk protein is quite evenly divided between cystine and methionine, while in cow's milk protein the sulfur is largely in the form of methionine. A possible relationship between this difference in sulfur distribution and the relative nutritive value of the milks of the two species is discussed.

ADDENDUM

Since this paper was submitted for publication, a private communication has been received from Dr. R. J. Block, stating that phenylalanine, threonine, leucine, and valine also occur in cow's milk and human milk proteins in approximately equal amounts. In confirmation of our results (Table VI), Block finds that human milk proteins yield somewhat more sulfur, arginine, tryptophane (and isoleucine) and considerably more cystine than do the proteins of cow's milk.

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SYDENHAM'S CHOREA

Preliminary Report of Three Cases Successfully Treated with Vitamin B_6

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NUMEROUS methods of treating chorea have been and are still being used. Some of them, such as the use of nirvanol and pyrotherapy of various types, shorten the course of illness but are attended with some danger and considerable discomfort to the patient.

In view of the satisfactory use of vitamin B_6 (pyridoxine hydrochloride), as reported in the treatment of nervousness and irritability,[1] epilepsy,[2] and especially in Parkinson's disease,[3, 4] one of us (J. S.) conceived the idea that this therapy might be of value in chorea. To date, three cases of Sydenham's chorea which were successfully treated with B_6* and were entirely devoid of any deleterious effects are being reported.

CASE REPORTS

Case 1.—M. C. was admitted Nov. 28, 1940, with a history of twitchings of the left hand for three weeks prior to admission, with accentuation of the movements as time elapsed. Her past history was one of frequent colds and occasional sore throats but otherwise was negative. The family history was negative.

Physical examination revealed an 8½-year-old white female weighing 48 pounds. Her tonsils were moderately enlarged and cryptic. A loud systolic murmur was audible at the apex. Irregular movements of the left upper extremity were easily detected.

Urine, Vollmer patch test, blood count, blood chemistry, carbon dioxide combining power, and several blood sedimentations were all within normal range.

An x-ray of the chest and an electrocardiogram did not reveal any definite pathology.

A diagnosis of Sydenham's chorea was made.

The child was placed in bed and given ferrous sulfate, 3 gr. three times daily, 25 mg. of ascorbic acid three times daily and 3 teaspoonfuls of cod-liver oil daily.

Since no improvement was noted and the twitchings were becoming more marked, on December 2, pyridoxine was begun, 3 mg. being given orally four times daily. Two days later, some improvement was manifested, enough so that on December 5 the parents of the child commented on the change. The improvement became more marked daily and on December 8, the dose was decreased to 3 mg. three times daily and continued for six more days, for a total dosage of 180 mg. By this time (December 14) the improvement was very marked, and it was felt that no further medication was necessary. Two days later, no further evidence of chorea could be detected, it thus having taken eighteen days to secure complete clearance.

Case 2.—V. L. was admitted Feb. 18, 1941, with a history of an attack of rheumatic fever with polyarthritis and carditis about four and one-half years previously which had been followed by recurrent attacks every winter. About two and one-half

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*The pyridoxine hydrochloride was supplied through the courtesy of Dr. C. F. Church, Medical Director of E. R. Squibb & Sons, New York, N. Y.

years before admission, he began to develop attacks of purposeless movements, and these have been recurring, each episode lasting from four to six weeks. The last attack was correlated with a tooth extraction which had occurred three weeks prior to admission and had been followed in two weeks by generalized twitchings of the body.

His past history revealed that he had had a tonsillectomy and pertussis at the age of 3 years, varicella at 5 years of age, mumps at the age of 6 years, and rubeola at 7 years of age. He had had occasional sore throats and averaged about three colds a years.

The family history was negative.

Physical examination revealed an 11-year-old white male child weighing 71 pounds. His heart was enlarged with the apex in the sixth interspace, 2.5 cm. outside the midclavicular line, and a double murmur was audible at the apex and associated with a booming P_2. There were coarse involuntary movements of the head and grimaces of the face. The purposeless, jerky movements of the upper extremities were so marked that the whole body appeared to be involved. These movements were also noted in the lower extremities, especially on the right side. The remainder of the examination was negative.

The urine, Vollmer patch test, blood culture, and chemistry were negative. The blood count showed a hemoglobin of 85 per cent; W. B. C., 13,000; polynuclears, 56 per cent; and lymphocytes, 44 per cent.

An electrocardiogram revealed a prolonged P-R interval, and an x-ray of the chest showed a slightly enlarged cardiac shadow.

The sedimentation rate was 70 mm. for the hour and the Weltmann reading was 4.

A diagnosis of chorea and rheumatic endocarditis (active) was made.

On February 27 pyridoxine was started. One cubic centimeter (25 mg.) was given intravenously and then 2 c.c. were given daily, except on March 3, when it was omitted through an oversight. On March 4, improvement was becoming evident, and the boy himself said that he felt better after the injections. By March 6, the improvement was so marked that the mother stated that she had never seen such rapid improvement before, for in previous attacks it had been weeks before any improvement had been noted. In view of the marked change for the better, the dosage was reduced to 1 c.c. daily and continued until March 12, when no further evidence of chorea could be detected, although the persistence of the elevated sedimentation (72 per hour) indicated further rheumatic activity.

Thus the chorea had responded within four days after 175 mg. of B_6 had been given and was fully cleared thirteen days after therapy had been started. The total dosage used was 425 mg. (17 c.c.).

CASE 3.—P. F. was admitted March 11, 1941, with a history of chorea with associated cardiac involvement since 4 years of age.

His first attack occurred in March, 1935, with restlessness and involuntary movements, and when he was admitted on May 22, even his speech was affected, and a mitral insufficiency was detected. He received no therapy, and the first sign of any improvement was on July 3, 1935, or forty-one days after admission. However, he was not ready for discharge until July 27.

His second attack occurred on May 7, 1938, and on May 14 he was admitted. Typhoid therapy was given from May 24 to 31 inclusive, the dosage ranging from 0.1 to 0.7 c.c. No improvement was noted, and therefore on June 8 another course was given, starting with 0.4 c.c. and working the dose up to 2 c.c. on June 17, but still no improvement was noted. A suspicion arose that this might not be a chorea, but on June 21 the neurological service substantiated the diagnosis. The child was kept in the hospital until July 8, when he was sent to a convalescent home, with the condition unchanged.

On Feb. 2, 1939, he was readmitted with a history of very mild movements since his last discharge. He was given no therapy and was discharged on February 18 with the condition unimproved.

His fourth admission was on July 12, 1939. He was given calcium chloride, 20 to 30 gr. three times daily, from July 13 to 26 with no improvement. From then on, bed rest and sedation were continued until August 29, when the condition showed slight improvement. Thus it had taken forty-seven days before any improvement could be noted. However, movements were still present, and on August 31, he was sent to the country, only partially improved.

His present attack, which was his fifth, had started two weeks before his admission with twitchings of the face and left extremities, and these movements had become progressively worse.

His past history revealed that he had developed normally. He had had an appendectomy at the age of 3 years, a tonsillectomy at 5 years of age, rubeola at 4 years of age, pertussis at the age of 6 years, mumps at 9 years of age, and also had had occasional sore throats and colds.

The family history was negative, and there were no other children in the family.

Physical examination revealed a 10-year-old white male weighing 71 pounds. Although he appeared well developed, he was moderately undernourished. Facial grimacing and involuntary movements of the extremities, especially on the left side, were marked. The cervical glands and left submaxillary gland were enlarged. A soft systolic murmur was audible over the precordium. No abnormal reflexes were elicited. During his stay his temperature, pulse and respiration were normal.

The urine, Vollmer patch test, blood count, chemistry, Wassermann, sedimentation, and Weltmann tests were all within normal.

An x-ray of the chest revealed a slight convexity of the left cardiac border; and an electrocardiogram revealed a slurred R wave in Leads I and IV and an inverted T wave in Lead III.

In view of the above, a diagnosis of chorea with associated mitral insufficiency was made.

On March 12, pyridoxine was started, 10 mg. being given orally three times daily. On March 16, four days after commencing medication, improvement was noted and this continued very slowly. Therefore, after the patient was kept on this dosage ten days, the dosage was increased to 20 mg. three times daily and continued for four days. At this point, the condition appeared stationary, so that from March 26 to 31 (six days) 30 mg. daily were given intravenously, and further improvement was noted. At this time, only very slight twitchings remained, so the boy was then placed again on oral medication, being given 15 mg. daily until April 8, when the patient became devoid of any movements. Thus it had taken twenty-eight days to clear this case.

This case was very interesting from the standpoint of the previous treatments, none of which had been effective, and improvement either was not noted or did not occur until forty-one to forty-seven days after onset of the specific treatment. Under the present therapy, improvement was noted after four days and continued very slowly with periods of apparent standstill. The improvement was gradual and the therapy finally resulted in a complete cure in twenty-eight days, a result which had never been obtained before in this case. Thus even the case which had been resistant to all previous treatments responded to pyridoxine after 840 mg. had been given.

DISCUSSION

The amount of B_6 necessary for a satisfactory response varied with each of the three cases, requiring from 180 to 840 mg. It was noted that the improvement under B_6 therapy was not discernible until the

patient had been under treatment for several days, and that the improvement was at first gradual, causing a diminution in the intensity of the involuntary movements and a feeling of general comfort and restfulness. The early subjective improvement was called to our attention by the voluntary verbal expressions of the patients. This was especially well illustrated in Case 2, in which the boy actually asked for the injections, apparently looking forward to them with great pleasure, because he claimed that he felt very much better after each one that had been given him.

Once the improvement began, the increment of amelioration was progressively increased, so that changes for the better could be noted almost daily. Even in Case 3, which previously had always been resistant to therapy, the changes for the better were progressive and constant, although slower than in the first two cases.

No reactions of any kind were encountered nor should they be expected.[5]

In view of the simplicity of the treatment and the lack of the necessity for constant observation and expensive laboratory work, this therapy lends itself admirably to home care, and thus reduces the general expense and hardships both to the individual and to the community.

In addition, the marvelous response of these patients to B_6 calls forth the observation that one of the etiologic factors in chorea may very well be that of a vitamin deficiency.

SUMMARY AND CONCLUSION

Three cases of Sydenham's chorea successfully treated with B_6 are reported.

In all of the cases, subjective amelioration apparently preceded but was soon followed and closely associated with progressive objective improvement.

The conclusion is reached that chorea may be primarily a vitamin deficiency, especially of the B_6 factor.

The ideal therapy for any condition would be one that gave successful results quickly, was easily and painlessly administered, had no harmful or discomforting effects, and was inexpensive so as to be applicable on a large scale and within the reach of everybody. All these objectives seem to have been fulfilled by the B_6 in the above cases. It is appropriate to add that caution should be exercised in accepting any preliminary reports of cures by any therapeutic procedures until full verification by additional reports is forthcoming.

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COAGULATION DEFECTS IN INFANCY AND CHILDHOOD

The Frequency of Hypoprothrombinemic States and Their Treatment With Vitamin K

A Reclassification of Hemorrhagica Hypoprothrombinemia Neonatorum

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DURING the preceding twelve months, a number of cases of defective bleeding and coagulation states were referred to the Children's Hospital for examination. Every case was thoroughly investigated, and many were found to fall into the group of hemorrhagic diseases due to a state of hypoprothrombinemia. Despite adequate treatment, several of these patients failed to respond, and at post-mortem examination the reasons could be clearly seen. Because these cases represent a cross section of an average children's hospital, it is believed to be of interest to report the frequency with which hypoprothrombinemia occurs. All the patients reported on here are those whose admissions were advised for prothrombin studies. A representative group has been selected (Table I).

CASE REPORTS

In each of the cases the prothrombin concentrations were determined according to the method of Quick, using whole venous plasma which had been adequately oxalated. The determinations were performed within two hours after obtaining the blood. When the clotting times had been obtained, the results were converted into a concentration by the use of the Quick dilution curve formula.[1] In the brief discussion of the cases, the other routine laboratory procedures, although performed, have been omitted because of their universal acceptance as criteria of certain diseases. The diagnoses offered were all substantiated by these tests. Frequent reference was made to the excellent paper by Quick[2] on the differential diagnosis of diseases affecting the coagulation mechanism.

Cases 1, 2, 3, and 4 are grouped together because they represent the common syndrome known as hemorrhagica hypoprothrombinemia neonatorum. Strangely, Case 2 had no deficiency of prothrombin and recovered without therapy. However, at the age of 2 months the infant succumbed to bronchopneumonia. The other cases were typical of the type admitted to the hospital and all responded quickly to therapy with vitamin K. Unless otherwise mentioned, the dose of vitamin K has been kept at 2,000 Ansbacher units twice daily, of synthetic aqueous vitamin K by hypodermic injection. In the Children's Hospital the most

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From the Children's Hospital.

TABLE I

CASE REPORTS OF COAGULATION DEFECTS IN INFANTS AND CHILDREN

(Although performed, all laboratory work necessary for proper diagnosis has been omitted from the chart below.)

CASE	NAME	AGE	SEX	COLOR	SYMPTOMS	DIAGNOSIS	PROTHROMBIN CONCENTRATION (%)	TREATMENT
1	D. G.	10 days	M	W	Omphalorrhagia for 8 days	Hemorrhagic disease of newborn infant	33	8000 Thayer units conc. vit. K (oral), cure
2	B. R.	12 hr.	M	W	Purpura over face	Hemorrhagic disease	100	Spontaneous cure, 13 days
3	B. F.	3 days	M	W	Omphalorrhagia, dermatorrhagia, 12 hr.	Hemorrhagic disease	5 100	8,000 Ansbacher units (hypo.); cure immediate
4	C. McR.	2 days	M	W	Melena, 2 hr.	Hemorrhagic disease	5	8,000 Thayer units vit. K (oral); cure
5	M. M.	10 days	F	C	Jaundice, omphalorrhagia 8 days	Congenital intrahepatic biliary atresia	5	No treatment; died; post mortem confirmed diagnosis
6	V. C.	10 yr.	F	W	Jaundice, acholic stool, epistaxis, oral bleeding, hepatosplenomegaly, 6 mo.	Cirrhosis of liver, possible Banti's syndrome	36 5 5	6,000 units synthetic vit. K (oral) daily; transfusions; bile salts; died; post mortem showed Laennec's cirrhosis
7	R. R.	4 days	M	W	Bronze jaundice, 24 hr.	Erythroblastosis fetalis, icterus gravis neonatorum	75 100 100	8,000 vit. K,; transfusions; recovered
8	M. B.	3 mo.	F	C	Jaundice, acholic stools, 3 mo.	Syphilitic hepatitis	100	No treatment; died
9	B. B.	6 wk.	M	W	Ascites, dermatosis, hepatomegaly	Congenital syphilis	21	No treatment; died; post mortem showed gummatous infiltration of liver and spleen

TABLE I—CONT'D

CASE	NAME	AGE	SEX	COLOR	SYMPTOMS	DIAGNOSIS	PRO-THROMBIN CONCEN-TRATION (%)	TREATMENT
10	B. W.	10 days	F	W	Congenital vomiting, epistaxis, postoperative melena and epistaxis	Congenital jejunal obstruction	Not done	Surgery; 4,000 units vit. K_1 (hypo.); hemorrhage arrested
11	T. W.	6 days	F	W	Congenital vomiting, postoperative gastrointestinal hemorrhage	Congenital duodenal obstruction	Not done	Vit. K omitted; died
12	R. O'M.	5 yr.	M	W	Epistaxis, hematuria	Acute myeloblastic leucemia	65 91	4,000 units vit. K_1 (oral); no effect
13	J. M.	8 yr.	M	W	Multiple hematomas, 2 yr.	Hemophilia	100	Transfusions
14	W. G.	7 yr.	M	W	Hematoma of knee joint	Hemophilia	100	Transfusions
15	W. H.	7 yr.	M	W	Repeated hemoarthrosis	Undiagnosed (most likely hemophilia)	67 100	6,000 units daily for 2 wk.; not followed
16	D. Mc.	10 yr.	M	W	Repeated hemoarthrosis	Hemophilia	100	None
17	W. B.	2 yr.	M	W	Vague hemorrhagic episodes	Idiopathic nonthrombocytopenic purpura	100	None
18	B. D.	4 days	F	W	Cyanosis, listlessness	Intracranial hemorrhage	Not done	12,000 Almquist units vit. K_1 (oral); recovered
19	B. M.	4 days	M	W	Convulsions, refused feedings, bulging fontanel	Intracranial hemorrhage	Not done (yellow spinal fluid)	4,000 Ansbacher units vit. K_1 (hypo.); recovered
20	B. D.	2 days	M	W	Listlessness, refused feedings	Intracranial hemorrhage	Not done (yellow spinal fluid)	12,000 units vit. K_3; recovered
21	W. P.	20 days	M	W	Oral bleeding, diarrhea, opisthotonus	Intracranial hemorrhage, hemorrhagic disease	Not done; coagulation time over 4 hr.	2,000 units vit. K_3; expired in several hours; post mortem revealed cerebral hemorrhage

frequent source of bleeding is from the umbilical cord (Fig. 1). This may be accompanied by dermatorrhagia. In the nursery, gastrointestinal hemorrhage predominates.

Fig. 1.—Case 3. Typical hemorrhagica hypoprothrombinemia neonatorum in a 3-day-old infant. Dermatorrhagia of the right upper arm and omphalorrhagia can be seen. Prompt response to vitamin K was obtained.

Cases 5, 6, and 7 were grouped together because they represent varying degrees of liver damage. Case 5 was that of a 10-day-old infant admitted with jaundice and omphalorrhagia for the preceding eight days. The infant was in such poor physical condition that it died shortly after admission. It was possible to obtain a specimen of blood for study just before death. A prothrombin concentration of below 5 per cent was found. At post-mortem examination a characteristic congenital intrahepatic biliary stenosis was found, accompanied by evidence of liver damage. Case 6 was that of a 10-year-old white female who was sent into the hospital because of repeated attacks of jaundice for the preceding six months. Because of the jaundice and frequently occurring epistaxis, a prothrombin determination was ordered and the results showed a concentration of about 36 per cent. She was given 24,000 units of vitamin K concentrate orally and 8,000 units of synthetic vitamin K by hypodermic injection. Despite this large dosage, which was augmented by bile salts, the prothrombin concentration remained consistently below 50 per cent although no further evidence of hemorrhage was encountered. A diagnosis of hepatosplenomegaly and Banti's syndrome was made, and the patient, at the request of the parents, was sent home. She returned in four weeks with pneumonia and a hemorrhagic

effusion in the right pleural cavity. Purpura and epistaxis developed in a short time, and the patient's condition became critical. A prothrombin concentration of less than 5 per cent was found, and the patient was again placed on vitamin K therapy with bile salts. Despite three transfusions* and 32,000 units of 2-methyl 1-4 naphthoquinone orally, there was never a prothrombin concentration over 5 per cent of normal. After twenty-four days the patient died. A limited post-mortem examination revealed an advanced cirrhosis of the liver, hemorrhagic fluid in the abdominal cavity, and gross hemorrhage in both visceral pleurae. The failure of response to therapy with vitamin K was due to the marked liver damage.

Cases 8 and 9 represent different stages of liver damage encountered in congenital syphilis. Case 8 was that of a 3-month-old negro infant admitted with typical jaundice; at the time of admission a diagnosis of syphilitic hepatitis was made. For clinical interest a prothrombin determination was made and revealed a normal concentration. After the infant's death, a post-mortem examination revealed an early syphilitic cirrhosis. Case 9, however, clinically presented a picture of congenital syphilis without jaundice but with marked hepatosplenomegaly and ascites. A prothrombin determination was found to be 21 per cent of normal. Since the test was performed shortly before death, no therapy could be administered. These two cases are grouped together because they clearly show that a diagnosis of hypoprothrombinemia on a purely clinical basis cannot be made. The post-mortem examination of the second case revealed numerous gummatous lesions in the spleen and liver. Both these cases were confirmed by the accepted blood and tissue studies. This is in agreement with the recent work of Lucia and Aggeler.[3] Apparently the amount of liver damage will not determine the amount of hypoprothrombinemia.

A patient with icterus gravis neonatorum (Case 7) was admitted to the hospital at the age of 4 days. The characteristic bronzelike jaundice was noted. The hemogram revealed 8.5 Gm. of hemoglobin and 2,630,000 erythrocytes. Marked basophilia and moderate macrocytosis were noted. Blood Kahn and Laughlen tests were negative. Fifty thousand erythroblasts per cubic millimeter of blood were found. Culture from the umbilical cord produced no growth. The history revealed no evidence of jaundice in two siblings or in other members of the family. Although a normal bleeding and coagulation time had been found previously, the patient was given 2,000 units of synthetic vitamin K hypodermically immediately on admission, and this dose was repeated daily for the next three days. About twelve hours after admission, a prothrombin test was done and a concentration of 75 per cent was found. The infant received a transfusion of 60 c.c. of citrated blood the same

*A fourth transfusion was ordered, but it was found that the patient's serum agglutinated her own red blood cells. Whether or not vitamin K was responsible for this strange condition was not known.

day. The jaundice deepened and an icterus index was found to be 350 units. At no time in the subsequent stay in the hospital did the infant show any signs of petechial or purpuric hemorrhages. Several prothrombin concentrations were found to be normal. This patient was given a total of eleven transfusions while in the hospital and made an uneventful recovery in thirty-four days. All erythroblasts disappeared from the peripheral blood in twelve days. In this case, no claim is made that vitamin K cured the disease as others have indicated. It is felt that in erythroblastosis fetalis, it is common to encounter a state of hypoprothrombinemia, because the disease usually occurs during the period of physiologic hypoprothrombinemia. However, in extreme jaundice a transient liver damage does exist in addition to the obstructive jaundice. These infants are in constant danger of serious bleeding and vitamin K should be given in adequate doses. Transfusions are an important regime, however, and appear to tide the infant over until this abnormal state of hemopoiesis has disappeared. The ideal therapy should include vitamin K and repeated transfusions. It does not appear that vitamin K will restore this confused state of erythroblastosis.

Cases 10 and 11 are those of congenital obstruction of the gastrointestinal tract. In a 10-day-old infant (Case 10) a congenital jejunal obstruction was found on surgical exploration and was properly released. Because the infant was not seen until the postoperative state, a prothrombin estimation was not performed. Nasal and gastrointestinal hemorrhages developed about twelve hours after operation, and 4,000 units of synthetic vitamin K in sodium bisulphite solution were given hypodermically. The bleeding ceased shortly and the infant recovered completely. Case 11 came to surgery at the age of 6 days, at which time a diaphragm of mucous membrane obliterating the duodenum was found. Shortly after operation the infant began to vomit and pass gross blood per rectum. This patient was not studied for a prothrombin concentration preoperatively and consequently received no vitamin K, although a transfusion of citrated blood was given. The patient died within twenty-four hours. Autopsy revealed many small hemorrhages in the abdominal cavity at the site of surgery. The blood was not clotted well. It is safe to say that this may have been prevented had vitamin K been given preoperatively.

Almost all cases of terminal leucemia will develop hemorrhage into the skin and from other sites. This is usually attributed to a thrombocytopenia. In many of these cases at the Children's Hospital, prothrombin studies were usually normal. However, one patient (Case 12), with hematuria and epistaxis, showed a prothrombin elevation from 65 to 95 per cent with 4,000 Almquist units of concentrated natural vitamin K in peanut oil.

Four cases of proved hemophilia were studied (Cases 13, 14, 15, and 16). In one (Case 15), a concentration of 67 per cent of normal was

found. Although the test was rechecked, no source of error could be found in the technique. This patient was given 6,000 units of concentrated vitamin K in peanut oil daily for two weeks, and when examined again, he was found to have a normal concentration. Because this patient has not returned to the dispensary, he has not been followed. The rest of the cases all were found to be normal in respect to prothrombin.

A case of idiopathic nonthrombocytic purpura was studied and a normal concentration of prothrombin was found (Case 17).

The last four cases were those of intracranial hemorrhage, all of which were thought to be a part of a generalized hemorrhagic tendency. Two of the cases were examined outside the hospital in consultation and no prothrombin estimations were made. Three cases made an easy recovery with vitamin K therapy. The fourth case (Case 21) was exceedingly interesting because it represented the development of an intracranial hemorrhage while the child was in the hospital.

Fig. 2.—Case 21. Development of intracranial hemorrhage in a 20-day-old infant with severe diarrhea. Marked opisthotonus can be noted. Subsequent therapy with vitamin K was of no value. Post-mortem examination revealed massive hemorrhage into the ventricles.

A 20-day-old white male infant was admitted to the ward service on recommendation of the physician who had delivered the mother. Because the child had been brought some distance to the hospital and was accompanied by a person unfamiliar with the case, a detailed history could not be obtained. During the first thirty-six hours in the hospital, the infant had fourteen loose, watery, green-yellow stools. Dehydration was treated with adequate parenteral fluid. Upon social service investigation into the post-natal condition, it was found that there had been some vague bleeding from the oral cavity associated with what

appeared to be thrush. This had occurred at the age of 4 days. No evidence of frank hemorrhage was noted by the parents. The dietary history of the mother during her prenatal condition was extremely poor. No vitamin K had been given. About thirty-six hours after admission the infant developed a marked opisthotonus without any signs of meningeal irritation (Fig. 2). A lumbar puncture was performed and gross blood in the spinal fluid was noted. The pressure was increased. Because of the possibility of error in technique, a cisternal tap was done and the same hemorrhagic fluid obtained. A diagnosis of intracranial hemorrhage was made and the infant was given 2,000 units of synthetic vitamin K intramuscularly. At the same time a small transfusion of citrated blood was given. Just before the transfusion, as much blood as could be obtained was sent to the laboratory where it was noted that the blood remained liquid for nearly four hours. Despite all therapy the patient died fifty-four hours after admission. At post-mortem examination fluid blood was found in many of the body cavities. The brain surface was covered with many petechial hemorrhages and the convolutions were flattened. On opening of the brain, the ventricles were found to be enormously distended with poorly clotted blood. There appeared to be some evidence of a previously organized clot from which the recent hemorrhage had started. Unfortunately, because of the rapidity of occurring events, a prothrombin concentration had not been ordered. However, this appeared to be a case of delayed hemorrhagic disease of the newborn infant, with intracranial hemorrhage superimposed on a previous interventricular hemorrhage. The diarrhea undoubtedly contributed to the hemorrhagic state and probably depressed the prothrombin level low enough that a poorly formed clot at the site of a previous hemorrhage was dislodged and further hemorrhage started. It is possible that hemorrhage had continued into the ventricle from birth, and that when sufficient bleeding had occurred to distend the ventricle, opisthotonus suddenly developed.

DISCUSSION

In retrospect, it is easily seen that many diseases characterized by a defective clotting mechanism do not fall into the class of hypoprothrombinemic hemorrhages. About 43 per cent of the cases usually characterized by a bleeding defect were found to be associated with some degree of hypoprothrombinemia. This does indicate that bleeding due to a depression of the prothrombin of the blood is very common and should be intelligently considered in the differential diagnosis of clinical hemorrhage.

A purely academic approach to a differential diagnosis of coagulation defects can be had by referring to the outline suggested by Quick.[2] The laboratory detection of hypoprothrombinemia needs no detail at present. Available for most laboratories are the methods of Quick, Smith, Warner and Brinkhous, Kato, Bray, Glavdin, etc. If venous plasma is available,

the Quick method has stood the test of accuracy well enough to be universally adopted. Where capillary blood is obtained, then a modification of the Quick method such as the Kato or Bray method can be used. These latter tests have to be compared to a normal control. The two-stage method of Smith and associates must be retained for the well-equipped laboratory because of the detail involved in its perfection. Fig. 3 indicates roughly the underlying principles of the various tests.

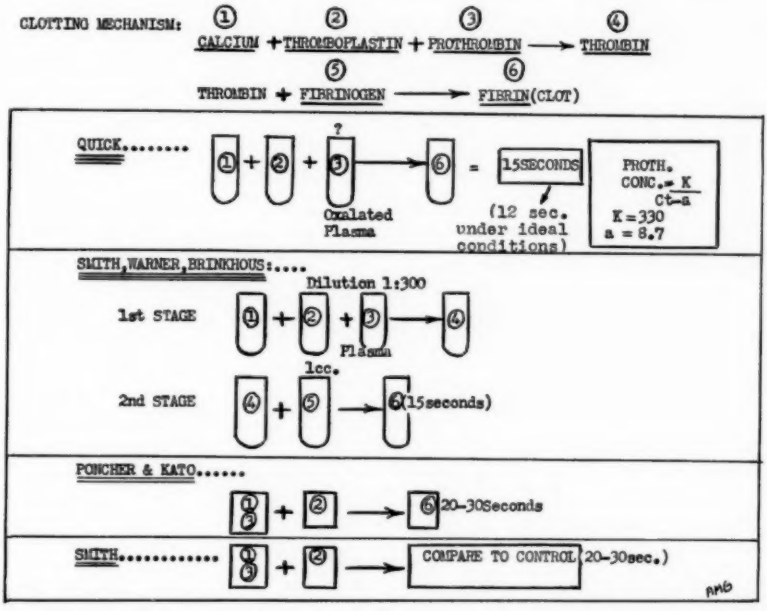


Fig. 3.—Outline of prothrombin determinations. (Only the underlying principles of the many tests for prothrombin in the blood are presented. The exact techniques can be found in many recently published periodicals or in the original papers.)

A simple classification of the various disorders resulting in a state of hypoprothrombinemia is offered in Table II. Three great groups are noted. The disease called toxic sweet-clover hay disease occurs only in cattle and has no counterpart in the human being. The next group are those diseases in which the liver is damaged to a degree sufficient to decrease the elaboration of prothrombin. In this group vitamin K does not cause a prompt response and many times does not correct the disorder. The largest group of diseases are those due to a K-avitaminosis. Subdividing this are the two groups of dietary deficiency and faulty absorption. Most of the diseases encountered in late childhood and adult life which are associated with a hypoprothrombinemia will be found in the latter group. Practically any disease in which there is either an obstruction or diversion of bile away from the intestinal tract will result, in the course of seven or eight days, in some degree of low-

TABLE II

CAUSES OF HYPOPROTHROMBINEMIA

K-AVITAMINOSIS		LIVER DAMAGE	TOXINS
DIETARY	FAULTY ABSORPTION		
1. *Physiological hypoprothrombinemia*	1. *Obstructive jaundice*	1. *Chloroform poisoning*	1. *Toxic sweet-clover hay disease* in cattle
2. *Hemorrhagic disease of newborn infant*	2. Biliary fistulas	2. *Acute yellow atrophy*	
3. Prolonged vomiting of newborn infant	3. Congenital obstruction in high gastrointestinal tract	3. Postanesthetic liver damage	
	4. Intestinal obstruction	4. Cirrhosis	
	5. Gastrocolic fistula		
	6. Sprue		
	7. Regional ileitis		
	8. Ulcerative colitis		
	9. Intestinal polyposis		
	10. *Erythroblastosis* fetalis		
	11. Prolonged diarrhea		

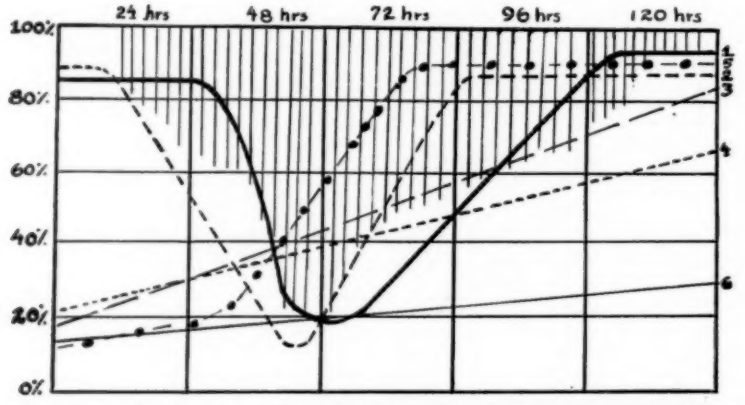


Fig. 4.—A comparison of prothrombin levels in the newborn infant, according to various investigators. *1.* ———, Quick and Grossman, Waddell and Guerry, Smith and associates, Dam and Plum, MacPherson; *2.* – – – –, Nygaard; *3.* — — —, Hellman and Shettles; *4.* – – – –, Poncher and Kato; *5.* —,—,—, Kove and Siegel; *6.* ———, Smith, Warner, and Brinkhous. (These concentrations are only approximate and are presented only to give a general idea of the results that have been obtained.)

ered prothrombin level. Likewise, any disease of the gastrointestinal tract in which the mucous membrane and associated tissues are destroyed may develop a state of hypoprothrombinemia.

Erythroblastosis fetalis, especially icterus gravis neonatorum, has been found to be associated almost always with a decrease in the available prothrombin. If this is due to liver damage, then there would not be a prompt response to vitamin K therapy such as is usually seen. Therefore, this disorder of the newborn infant has been placed in the category of those diseases due to a faulty absorption of vitamin K.

It has been well established that there exists a condition of physiologic hypoprothrombinemia of the infant.[4] Most investigators are in agreement concerning prothrombin concentration in the newborn infant (Fig. 4). It is during these first few days of life that the average baby is in danger of hemorrhage. The cause of this disorder is the failure of the fetus to store sufficient prothrombin for use after the first twenty-four hours of life. At the end of the first day of life, the prothrombin level drops down to lower strata than ordinary. By the third day most babies will have a normal concentration. Some will be delayed until the fifth day. Bacterial synthesis in the gastrointestinal tract produces enough vitamin K to begin the elaboration of prothrombin. This bacterial synthesis is produced when the infant takes its first food. Consequently, the earlier feeding of infants is to be recommended. It has also been sufficiently established that hemorrhagic disease of the newborn infant is due to a state of low prothrombin plus a certain factor of birth trauma. The cause of the hypoprothrombinemia is a failure of the restoration of the prothrombin concentration due to delayed hepatic and biliary function. In the premature infant this delay is even greater.

TABLE III

HEMORRHAGICA HYPOPROTHROMBINEMIA NEONATORUM

SUBCLINICAL	CLINICAL		
	INTERNAL	EXTERNAL	
		MAJOR	MINOR
Retinal hemorrhage Subarachnoid hemorrhage Spinal fluid xanthochromia Serous meningitis of newborn infant Increased spinal fluid pressure Transient melena neonatorum	*Intracranial hemorrhage* Intraperitoneal hemorrhage *Intra-adrenal hemorrhage*	*Melena* *Hematemesis* Dermatorrhagia *Omphalorrhagia* Nasal and oral surgical hemorrhage genitourinary	*Cephalohematoma hemorrhage.* *into sterno*-cleidomastoid muscle

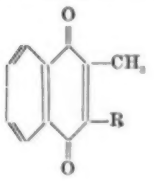
From practical experience, and the establishment of a definite etiology, it is advisable to reclassify these hemorrhages of the newborn infant into a simple group of symptom disorders. As indicated in Table III, two forms of the disease must be recognized, clinical and subclinical. The subclinical forms are due to the appearance of petechial hemorrhages in the serous and mucous membranes of the body. They usually escape detection clinically or they may be diagnosed wrongly. In the eye, an incidence of 12.3 per cent of retinal hemorrhages has been found.[5] The transient xanthrochromatic spinal fluid and increased spinal fluid pressures encountered in many infants are caused by petechial subarachnoid hemorrhages. During these first few days a transient melena can be found due to the appearance of petechial hemorrhages throughout the gastrointestinal tract. With the usual normal restoration of the prothrombin level by the fourth day, these petechial hemorrhages cease

spontaneously. However, should there be some failure of this restoration to occur, these small hemorrhages become gross hemorrhages and the disease becomes recognized as the clinical form. These hemorrhages are caused by a failure of the petechial hemorrhages to disappear because of a faulty clotting mechanism. These hemorrhages can be external or they can be internal if they occur into closed cavities. If they are external it is a simple matter to recognize the common hematemesis and melena. This form of bleeding is encountered in the nursery. At the Children's Hospital, however, the most common form of bleeding is from the umbilical cord and into the skin (Fig. 1). These forms can be considered as major clinical forms of the disease. A minor form of hemorrhage can occur into the sites most frequently traumatized at birth, i.e., the subperiosteum of the scalp and the belly of the sternocleidomastoid muscle. These forms of hemorrhagic disease of the newborn infant are noted not at birth, but at the time the coagulation mechanism becomes distorted, on the third and fourth days.

By the same mechanism of external bleeding, hemorrhage can occur into closed cavities such as the peritoneum, adrenal gland, and intracranial vault. It is when this form of bleeding disease is included that the mortality rates become exceedingly grave. Symptoms of intracranial hemorrhage which appear before the infant is 48 hours of age usually indicate evidence of a frank laceration of a blood vessel, and this form of the disease should not be included in this classification. According to older classifications, hemorrhagic disease of the newborn infant is rather rare. However, when a reclassification is offered which includes the aforementioned varying types of hemorrhage, the disease becomes fairly common.

TABLE IV

VARIOUS FORMS OF NATURAL AND SYNTHETIC VITAMIN K

VITAMIN K	
	K_1: Alfalfa 2 methyl-3phytyl-1, 4-naphthoquinone 1 mg. = 250-500 units
	K_2: Fish meal 2-methyl-3(R = C_{35})-1, 4-naphthoquinone 1 mg. = 300 units
	K_3: Phthiocol 2-methyl-3-hydroxy-1, 4-naphthoquinone 1 mg. = 200-500 units
	K_4*: 2-methyl-1, 4-naphthoquinone 1 mg. = 2,000 units
	K_5: 2-methyl-4 amino-1, naphthol hydrochloride

*Commercial preparations are: (oral) Thyloquinone, Proklot, Kayquinone, Quino-Thrombin, Klotogen, Cerophyl; (parenteral) Hykinone, Synkamin.

No new methods of therapy can be offered from the results obtained in this small series. However, it is recommended that the physician familiarize himself with the many different media of administration of vitamin K as they are commercially distributed (Table IV). From practical experience it has been found that vitamin K is best given in the aqueous extract by hypodermic injection in unit doses of 2,000 units.

For the prevention of hypoprothrombinemia in the newborn infant, 2,000 units (Ansbacher) daily for two days by hypodermic injection will usually protect the infant. The premature baby should be given the vitamin K for two more days. For the treatment of hemorrhagic disease of any form, 2,000 units twice daily by hypodermic injection until the prothrombin concentration has returned to normal will be adequate. If no liver damage is present, the arrest of the hemorrhage will be prompt. In hypoprothrombic states of older children, 100 units per pound of body weight daily in divided doses, with 5 grains of bile salts for each 2,000 units, will suffice. This is best given orally unless the patient is unconscious. In any condition of biliary obstruction, the prothrombin concentration will remain low until the bile flow is restored to normal conditions, so it is necessary to maintain therapy until that time. In these conditions it is necessary to perform repeated prothrombin determinations to determine the time for cessation of therapy. It has been found that hypoprothrombinemia will be corrected to a degree in from two to six hours following the adequate administration of vitamin K. Should there be a failure of this response, liver damage should be suspected. Successful therapy with vitamin K has been achieved when hemorrhage has been arrested, the clotting time restored, and the prothrombin concentration returned to normal. All potential states of hemorrhage should be treated as actively as frank hemorrhage.

SUMMARY

Twenty-one cases of varying bleeding disorders are presented because they represent the frequency with which hypoprothrombinemic states develop in infancy and childhood.

A report of laboratory and clinical detection of hypoprothrombinemia has been simply presented.

A reclassification of hemorrhagica hypoprothrombinemia neonatorum is offered which renders the disease fairly common.

A suggestion for correct therapy with vitamin K is made.

These case reports are presented with the permission of Dr. Joseph S. Wall, Chief of the Medical Staff, and the members of the attending and associate staffs of the Children's Hospital, Washington, D. C.

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TELLURITE REACTION

Further Study on One Hundred Consecutive Cases at the Steele Memorial Hospital

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SINCE Dr. Alfredo Manzullo,[1] of the Bacteriological Institute of the National Department of Hygiene at Buenos Aires, first recorded a method whereby the power of the diphtheria bacillus to reduce potassium tellurite could be used as the basis of an immediate diagnostic test for diphtheria, a considerable number of reports have been made regarding its use, with somewhat conflicting results. In the first work done by Dr. Manzullo, particulars are given of seventy-five suspected cases of diphtheria. In thirty-five of them the immediate tellurite reaction, the provisional clinical diagnosis, and the bacteriologic culture were all positive; in thirty-four they were all negative. In two cases a positive tellurite test was confirmed by positive culture, although clinical diagnosis was negative. In one case the tellurite test was negative as was the culture, while the clinical diagnosis was positive. In three cases the tellurite test was negative when the culture was positive, and in two of these, the clinical diagnosis agreed with the cultural findings. In no case was there a failure to confirm a positive immediate tellurite test by bacteriologic culture.

Later, Tomlin,[2] reported on forty-four patients, admitted to Leicester City Isolation Hospital, who were immediately investigated by clinical impression, by tellurite method, and by bacteriologic culture. Here it was found that: (1) of twenty-eight cases which proved to be diphtheria, obvious darkening was obtained in twenty-seven, and in the twenty-eighth case, darkening was suspected after ten minutes and definite after thirty minutes; (2) one case was finally diagnosed on clinical grounds as diphtheria, despite failure to recover the organism bacteriologically, this case showing darkening; (3) on bacteriologic and clinical grounds, fifteen were proved, not to be diphtheria. Nine of them however, did show darkening, an unexpectedly high number of what might be called "false positives." An attempt was also made, with no consistent result, to correlate the depth of darkening with the rate, the age of the solution, and the day of the disease. Tomlin summarized his work by stating that "a negative result is of value in that it supposes, with great accuracy (100 per cent in this series, 92 per cent in that of Dr. Manzullo), that the disease is not diphtheria." He goes on to suggest it is unlikely that any case of diphtheria would be missed, should only this test be used, if the technique is not at fault.

Other workers, namely Tombleson and Campbell,[3] examined by the immediate tellurite test 200 cases of pharyngeal infection with exudate,

and obtained data corresponding with the bacteriological diagnosis in 67.5 per cent of the cases and with the clinical diagnosis in 77 per cent. Definite blackening occurred in 84.3 per cent of the cases of diphtheria, as well as in 46.8 per cent of faucial lesions due to other organisms. No blackening occurred in a small number of cases of diphtheria often of a severe type.

Cooper, Peters, Wiseman, and Davies[4] found 44 per cent false positive tests in their smaller series; they quote Hewitt's remark in explanation of these false positives: "Bacterial cultures are nearly always strongly reducing systems." Fox, Rhoads and Lack[5] applied the test to twenty-seven patients with throat infections. Seventeen yielded positive tests and positive cultures; nine patients with negative cultures had negative tests; and one false positive reaction occurred.

The purpose of preparing this series of 100 cases is to add to the literature further information concerning the advantages and disadvantages of the tellurite test, so that its ultimate value to practicing physicians far removed from laboratory facilities may be more accurately estimated. An attempt has been made to observe suggestions of previous writers for improving the technique of the test.

One hundred consecutive patients, each having a faucial or pharyngeal membrane, admitted to Steele Memorial Hospital for whatever cause, were subjects for this series. On the admission of each patient, a preliminary clinical impression was notated and a culture was taken. The type of membrane was described and it was also observed, upon examination of the throat, whether a particular pungent odor characteristic of diphtheria was present. Each case was tested with a 2 per cent potassium tellurite solution in 40 per cent glycerin, by means of dipping a sterile cotton applicator in the solution and touching it to the membrane, using great care to avoid the tongue. The membrane was then observed after ten minutes and again after thirty minutes. A record of the darkening and its degree was kept, and the clinical course during hospitalization was observed. At the time of discharge, when the results of the culture, the tellurite test, and the clinical course of the disease had been studied, a final diagnosis of the membrane was made. These diagnoses served as the basis for correlating the results of the 100 cases.

The tellurite solution was made up fresh every two weeks. In only two cases (72 and 76) was the solution older than two weeks, and this by mistake. The cultures were all grown on Loeffler's blood-serum media and stained with J. J. Kinyoun's[6] granule stain, in the laboratory of Denver General Hospital where all the culture work for the city and county of Denver is done. Only diphtheria growths were recorded. Membranes in throats with negative cultures were termed "membranes of other organisms."

The results of our tests on 100 consecutive cases of pharyngeal membrane are seen in Table I.

TABLE I

True positive reactions	48
True negative reactions	21
Undetermined membranes	2
Indefinite reactions	6
False negative reactions	16
False positive reactions	7

The true positive tests were those in which the three components of the diagnosis, namely, the culture, the final clinical impression, and the tellurite reaction, all coincided to make a final diagnosis of acute pharyngeal diphtheria membrane. Forty-eight true positive reactions indicate that of the 100 cases tested, only forty-eight of the sixty-eight which were actually acute diphtheria cases gave a positive tellurite reaction. The true negative cases refer to those in which the clinical course, the final clinical impression, and a negative reaction coincided to make a final diagnosis of some other cause for the membrane. Of the twenty-one such cases, fourteen had positive cultures but gave no signs or symptoms of acute diphtheria; these were classified as diphtheria carriers. Five membranes occurred coincident with clinical scarlet fever and were due to streptococci. One membrane was that covering a recent tonsillectomy fossa and gave a negative culture although the patient had previously given positive cultures and was classified as a carrier; one membrane gave a negative culture and was classified as a simple postnasal discharge.

Strictly speaking, the fourteen cases in this group which gave positive cultures should, according to the original idea of the test, have produced some color change, singe organisms were present. This was discounted, however, since acute diphtheria only is being considered.

Sixteen cases in which the final diagnosis, based on positive culture and clinical course, left no question that the case was one of acute diphtheria, even though the tellurite test remained negative, were called false negatives. This group indicates that 23.5 per cent of the sixty-eight cases which were finally diagnosed as acute diphtheria would have been missed if the tellurite test alone had been relied upon. It is interesting to note that in ten of these sixteen cases the typical diphtheria odor was present.

When a positive tellurite test was present despite a negative culture and a negative clinical course, which constituted the basis for a final diagnosis of "membranes of other organisms," the case was termed a false positive. This group of seven patients, whose cases constitute 9.3 per cent of all that either tested positively or should have tested positively (forty-eight true positives, four indefinite reactions, sixteen false negatives, and seven false positives), would have been given antitoxin without needing it, had only the test been relied upon. Here also it is interesting to note that in all of these seven cases there was an absence of the particular diphtheria odor mentioned above. In only one case

(94), finally diagnosed as Vincent's angina, was any odor present at all, and this was a foul odor completely unlike that characteristic of diphtheria.

In order that error might be kept at a minimum, the cases in which there was the slightest degree of doubt about classification of the membrane or evaluation of the darkness of the test were placed entirely by themselves and considered as "undetermined membranes" or "indefinite reactions." The two undetermined membranes occurred because an incomplete study was made and a final diagnosis could not be determined. Both of these patients had positive cultures but none of the typical odor previously described. Although both patients gave negative tellurite reactions, and may well have been carriers, it was considered advisable to classify them by themselves since their subsequent clinical course was not followed. Of the six patients who gave "indefinite reactions," four were finally diagnosed acute diphtheria and were treated as such, while the tellurite reaction was recorded as only slight on both ten- and thirty-minute reactions. It is conceivable that these patients would have been given antitoxin had the test been relied upon completely and therefore would have been added to the number of true positives, making it fifty-two instead of forty-eight. The other two patients in this group showed no signs or symptoms of acute diphtheria despite their positive cultures, and they were treated as diphtheria carriers. These might have been added to the group of cases called false positives.

TABLE II

FINAL DIAGNOSIS		ODOR TYPICAL (NO. OF CASES)	ODOR NOT TYPICAL (NO. OF CASES)
Diphtheria	68 cases	48	
Diphtheria			20
"Membranes of other organisms"	32 cases	1	
"Membranes of other organisms"			31

Table II gives a succinct picture of the relationship between the typical diphtheria odor and the final diagnosis. This table points out that of the sixty-eight cases finally diagnosed as diphtheria, forty-eight gave a typical diphtheria odor, while twenty of them had none. These twenty cases may be considered comparable to the sixteen false negative reactions previously mentioned. The only case which was classified under "membranes of other organisms" but which gave a typical diphtheria odor indicates a marked reduction from the seven cases classified as false positives.

It is quite obvious from the work which has been presented that the effort of Manzullo to provide a rapid clinical method for the diagnosis of diphtheria has not withstood the test of other experimenters. Sixteen false negative tests out of 100 consecutive cases are a sufficient number to disqualify the method almost completely. This group constitutes a greater percentage of false negative reactions than that found by any

other investigator. Seven false positive reactions coincide quite closely with the percentage of other investigators. The six indefinite reactions further disqualify the method because of the difficulty present in a few cases of any series of accurately evaluating the degree of darkening. Although forty-eight true positive reactions and twenty-one true negative reactions have been recorded in this series, the number in these groups is not large enough to allow one to base the final diagnosis in any case with a pharyngeal membrane on this tellurite test alone.

Worthy of mention is the group finally diagnosed as acute diphtheria which presented a typical diphtheria odor. These cases readily demonstrate how experienced practitioners away from laboratory facilities could rely as confidently on this one characteristic of diphtheria (typical odor) as they could on the immediate tellurite test.

We may conclude from these findings that the clinical impression plus the bacteriologic culture and the course of the disease should never be supplanted by the immediate tellurite reaction.

We wish to thank Dr. H. C. Becker, Dr. J. J. DeRoos, Dr. R. W. Moody, Dr. J. K. Pickens, Dr. H. T. Robertson, Dr. R. A. Swanson, and Dr. F. M. Swisher for their assistance in compiling the material.

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RHABDOMYOSARCOMA

Case Report

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John Warren, M.D., Detroit, Mich.

MALIGNANT tumors of skeletal muscle are very uncommon, although skeletal muscle makes up a considerable portion of the body.

Contributions to the study of this group of tumors had been very limited until Abrikossoff[1] and Ewing[2] shed considerable light on the histology of these tumors. Cappell and Montgomery[3] further enlightened us by clearly differentiating two forms of striated muscle tumors: (1) the rhabdomyomas—those showing definite cross striations in the tumor elements and (2) myoblastomas—those showing no cross striations. Gordon-Taylor[4] and De and Tribedi[5] have given us the latest complete reviews on this subject.

We are reporting our case because of the rarity of this lesion in infancy and early childhood, its appearance in a negro child (only one other case of rhabdomyosarcoma being reported in a negro[6]) and the location of the tumor mass with its extensive metastasis.

J. W., a 2-year-old negro child, was admitted to the pediatric service of the John Gaston Hospital on Jan. 16, 1941.

Present Illness.—The child had had a cough and a cold for about two weeks prior to admission to the hospital. He had been treated with home remedies but did not seem to improve. About ten days before admission his cough became much worse and he began to have difficulty in breathing. The child had no other concomitant symptoms. Because of marked progression of these symptoms, the parents brought the child to the hospital.

Past History.—The child was a normal, full-term baby. There was a normal feeding and developmental history. The child had been vaccinated against smallpox but had no other immunizations.

When he was 6 months old, the parents noted a mass about the size of a walnut in the right calf area. This mass grew slowly, and at the age of 1 year it was the size of a small egg. At this time the child was brought to the receiving ward of the John Gaston Hospital. The parents were advised to take him to the outpatient department for further study but neglected to do so. The mass continued to grow, and on this admission was about the size of an orange.

The child had had no other illnesses.

Family History.—There was no history of tuberculosis, cancer, renal disease, diabetes, venereal disease, or allergic diseases in the family.

Physical Examination.—The general appearance was that of a very acutely ill negro male child, aged 2 years, whose respirations were very rapid and difficult. Temperature was 101° F.; respiration, 48; pulse, 134. The head, eyes, and ears were negative. There was marked inspiratory dilatation of the alae nasi. The mouth showed very poor oral hygiene. The throat was negative.

On inspection of the lungs there was no evidence of lag. On percussion there was marked dullness to flatness over the entire right lung field both anteriorly and

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posteriorly. There were no changes on percussion over the left lung field. On auscultation the breath sounds over the right side were markedly diminished with inspiratory phase heard, but expiration seemed to be replaced by a wheezing, clicking sound. The breath sounds on the left side came through well, but here also was the same type of expiratory phase. The breathing was so difficult at times that sternal and intercostal retractions were present.

Examination of the heart showed tachycardia but was otherwise negative.

The liver was palpable about three fingerbreadths below the right costal margin. The spleen was questionably palpable. A mass was felt high in the left hypochondrium which was felt to be left kidney.

Genitals were normal.

Neurological examination was essentially negative.

Examination of the extremities showed a large globular mass about the size of a large orange involving the entire calf area of the right leg (Fig. 1). This mass was firm but not phlegmonous, and no areas of fluctuation were present. The mass seemed to move with the movements of the gastrocnemius group of muscles and did not seem to be attached to bone.

Laboratory Procedures.—On Jan. 17, 1941, red blood cells were 4,010,000; hemoglobin, 12 Gm.; white blood cells, 28,500; differential, normal; urinalysis, negative; blood Kahn test, negative.

It was thought that the tumor mass of the right leg was most likely sarcomatous and possibly a rhabdomyosarcoma with metastasis to the liver and lungs. The pulmonary picture suggested the possibility of fluid in the right chest cavity, but the expiratory obstructive type of breathing suggested blockage of the main stem bronchi particularly on the right side. The temperature and general appearance of the patient did not conform with that of a pneumonic process.

X-ray examination of the chest revealed multiple metastatic nodules in the left lung field and complete haziness of the entire right lung field suggestive of fluid. X-ray of right leg showed large tumor mass but no bony involvement (Fig. 2).

Because of the child's marked dyspnea oxygen therapy by nasal catheter was given. Otherwise, therapy was purely symptomatic. Surgery was consulted as to a biopsy of the tumor mass, and radiology in regard to radiation therapy. Neither of these procedures could be carried out since the child continued progressively downhill and died at 10:00 A.M., Jan. 20, 1941.

A necropsy was granted and was performed about thirty minutes after death.

Gross Examination of the Tumor (Fig. 3).—The mass was located at the junction of the upper and middle thirds of the right leg in the region of the calf muscles. It was freely movable and did not appear to be attached to the overlying skin. A line of cleavage and a fibrous capsule 1 mm. thick was found around the tumor. There were many fibrous and normal appearing muscle tags attached to it. The capsule was easily separated from the surrounding tissue but was adherent to the periosteum of the tibia. The periosteum could easily be stripped from the bone. The latter showed no evidence of involvement. The gastrocnemius and soleus muscles were represented by thin, atrophic muscle sheets stretched over the tumor just beneath the subcutaneous tissue. The enucleated mass was roughly spherical and measured 8 cm. in diameter. It weighed 148 Gm. and was soft in consistency. The cut surface was homogeneous, yellowish white in color, and friable. There were several small areas of necrosis and hemorrhage in the center of the tumor.

Gross Examination of Metastasis.—The right pleural cavity contained 100 c.c. of a serosanguineous fluid. There were many fibrous adhesions between the layers of the pleura, particularly at the apex. The left pleural cavity showed neither of these. The surfaces of both pleural cavities were covered by many soft, yellowish-white masses, varying in size from 0.5 to 3 cm. in diameter. Each mass had a thick pedicle. The masses were arranged in clusters like bunches of grapes.

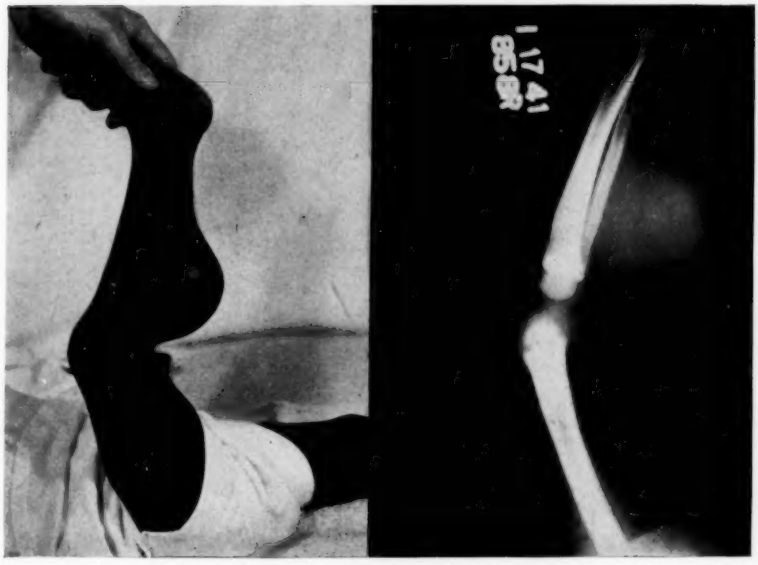

Fig. 1. Fig. 2.

Fig. 1.—External view of right leg showing the primary tumor.

Fig. 2.—Roentgenogram of right leg showing the soft tissue tumor. Note the absence of bone involvement.

Fig. 3.—Gross appearance of primary tumor. The left view shows the external surface with its thick capsule surmounted by normal striated muscle. The right view is a cross section. Note the central areas of hemorrhage and necrosis.

Both lungs were diffusely infiltrated with tumor, the right more extensively than the left (Fig. 4). The spherical masses were scattered throughout the lung tissue. These metastases were soft, yellowish white, and translucent and varied in size from 0.5 cm. to 3 cm. in diameter. The pulmonary tissue surrounding the tumor in the right lung had a uniform, bluish-red color and was atelectatic. The left tissue was crepitant and in general appeared to be normal. The mediastinum was filled with small tumor masses similar to those in the pleura.

There were no metastases in this case except in the lungs and mediastinum. The inguinal nodes were carefully examined, but no evidence of tumor was found.

Fig. 4.—Right lung with metastases.

Microscopic Description.—The tissues were fixed in 10 per cent formalin. Paraffin sections were stained with hematoxylin-eosin, Hansen's Van Gieson iron hematoxylin, phosphotungstic acid hematoxylin stains. The primary tumor was composed mainly of large, spindle-shaped cells with dark, eosinophilic cytoplasm (Fig. 5). The cytoplasm of some of these cells had a fibrillar appearance which resembled longitudinal striations. The nuclei were large and either round or oval and were located either centrally or eccentrically. The chromatin was in a lenticular arrangement, and mitotic figures were prominent. Some of these tumor cells occurred in parallel rows resembling fibers of striated muscle (Fig. 6). Cross striations could be demonstrated in a few of the larger and more mature cells with the phosphotungstic acid hematoxylin stain. These cells resembled myoblasts.

Large, bizarre, irregular and isolated cells were scattered throughout the tumor. Their cytoplasm was also acidophilic and granular. Their nuclei were either single or multiple and were vacuolated in many instances. The nuclei occurred in the periphery of the cell when multinuclear. Such cells are considered diagnostic of rhabdomyomata.

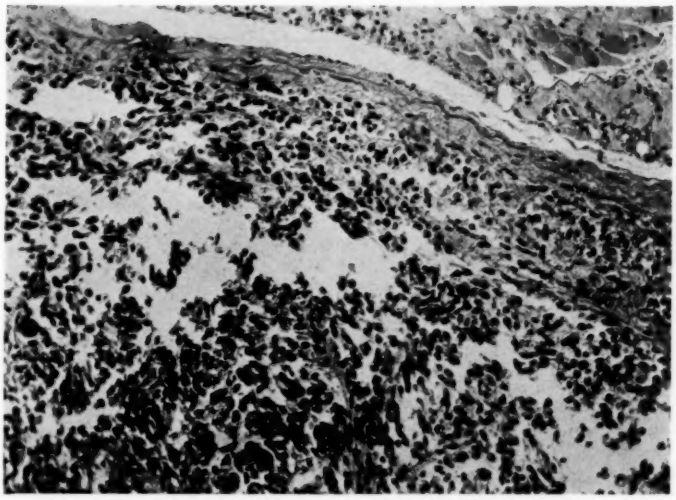

Fig. 5.—Low-power photomicrograph of primary tumor. Note normal striated muscle adjacent to the thick capsule. The parallel arrangement of the myoblasts can be seen. Several large, irregular cells are in the field.

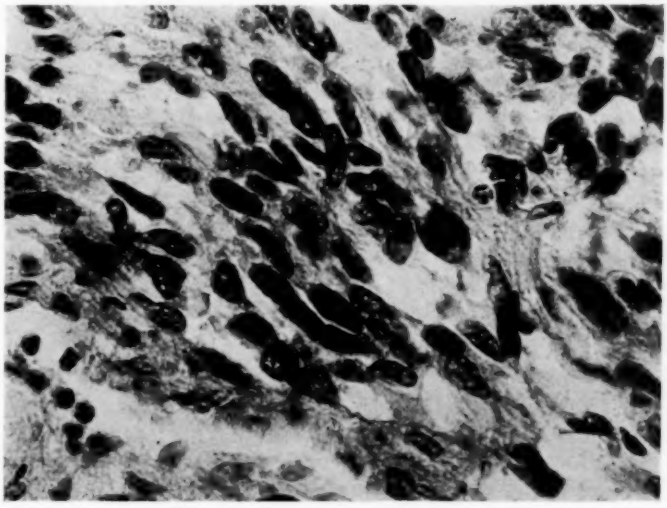

Fig. 6.—Photomicrograph (×700) showing parallel arrangement of myoblasts. Note the lenticular nuclei.

A third type of cell was seen rather infrequently in this tumor. These were enormous spindle-shaped cells with oval and eccentric nuclei. Some of these were multinucleated (Fig. 7). Their cytoplasm was also eosinophilic. The tumor cells were usually separated by a fine network of connective tissue.

The capsule was composed of dense, fibrous tissue. There were atrophic striated muscle fibers stretched over the tumor mass and attached to the capsule and the surrounding tissue.

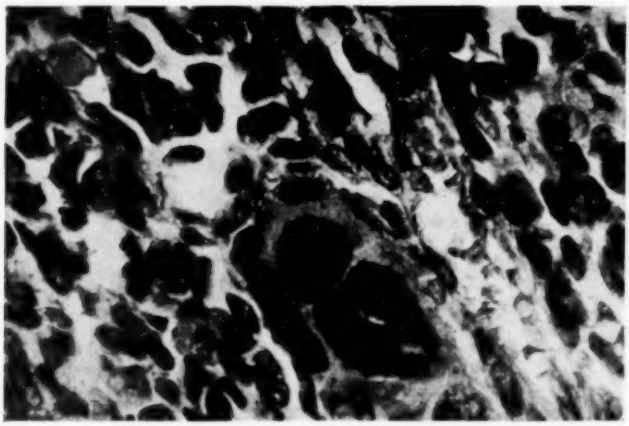

Fig. 7.—Photomicrograph (×700) showing a large, bizarre, multinucleate cell. Several vacuoles are in the nuclei.

The histologic picture in the pulmonary metastases was very similar to that in the primary lesion. It was interesting to observe the many tumor cells in the lymphatic channels, especially about the blood vessels. The alveoli were thickened and hyalinized in the region of the tumor. The lung tissue surrounding the metastases was atelectatic and hemorrhagic. The lymphoid tissue in the mediastinal lymph nodes was completely replaced by tumor tissue.

SUMMARY

A case of rhabdomyosarcoma of the gastrocnemius group of muscles with extensive metastases to the lungs is reported. This case is particularly interesting because of the age and race of the child and the location of the tumor with its marked metastases.

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PARAPERTUSSIS

Clinical and Serologic Observations

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Eldering and Kendrick[1, 2] and Bradford and Slavin[3] have independently described the isolation of an organism similar to *Hemophilus pertussis* from children suffering from severe cough. In both instances, the organism was found on cough plates obtained from persons suspected of having pertussis. Eldering and Kendrick isolated ten strains all of which were obtained from children who were considered to have clinical whooping cough. Bradford and Slavin isolated eight strains, two from infants with moderately severe clinical whooping cough and six from milder cases. Bradford and Slavin also studied a strain sent them by Eldering and Kendrick and strains received from Sauer. These strains were all found to be similar. The name *Bacillus parapertussis* was attached to this organism by Eldering and Kendrick.

Bacillus parapertussis is a small, nonmotile, Gram-negative coccoid bacillus morphologically indistinguishable from *H. pertussis*. On Bordet-Gengou ("cough plate") medium, the colonies appear earlier than those of *H. pertussis* but at first simulate the latter very closely. Both are pearly and have the appearance of drops of mercury. The medium about the colonies of *B. parapertussis*, however, soon becomes brown, and hemolysis is much more marked. At seventy-two hours, the colonies of *B. parapertussis* are much larger than those of *H. pertussis* and have a green cast.

The principal cultural characteristic of this organism, as opposed to *H. pertussis*, is its ability to grow on first subculture on plain infusion agar. It is not hemophilic. Two other differential cultural characteristics described by Bradford and Slavin are heavy growth on chocolate agar with production of catalase and growth on peptone-iron agar with production of brownish discoloration and catalase.

B. parapertussis shares common antigenic fractions with both *H. pertussis* and *Br. bronchiseptica*. Antiserum produced in rabbits by injection of any of these three organisms (or by natural bronchiseptica infection—"snuffles") will generally give cross reactions with the other two organisms. Absorption tests[2, 3, 6] have shown that homologous agglutinins are not well absorbed by a heterologous suspension, but heterologous agglutinins are well absorbed by a homologous suspension. (For example, parapertussis agglutinins in the serum of a rabbit which has been injected with *B. parapertussis* are not well absorbed by a

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Read at the meeting of the American Academy of Pediatrics Region IV, San Francisco, May 2, 1941.

TABLE I

SUMMARY OF CLINICAL RECORD

GROUPED IN REGARD TO TYPE OF HISTORY

CASE AND DATE	AGE	SEX	PAST HISTORY	EXPOSURE TO "WHOOPING COUGH"	COUGH			POST-TUSSIC VOMITING	NASAL DISCHARGE	DAY COUGH PLATE POSITIVE	CLINICAL DIAGNOSIS	SUBSEQUENT HISTORY
					TYPE	WHOOP	DURATION DAYS					
G. G. 7/38	14 mo.	M	—	None known	Paroxysmal not severe	—	23	Once	Purulent	10th day	Upper resp. infection	Negative
H. G. 3/39	7 yr.	M	—	None known	Paroxysmal not severe	—	7 Improving on 12th day	Twice	—	7th day	Mild whooping cough W.B.C = 9480 45% lymph.	Negative
G. N. 6/40	6 yr.	M	—*	None known	Paroxysmal severe	+	36	Repeatedly	—	10th day	Typical whoop. cough W.B.C. = 22,400 70% lymph.	Negative
S. R. 1/37	6 mo.	F	—	None known	Paroxysmal mild	—	14	—	Mucopurulent	2nd day	Upper respiratory infection	7 mo. later typical mod. severe whooping cough W.B.C. = 35,900 69% lymph.
H. S. 6/39	5½ mo.	F	—	None known	Paroxysmal mild	—	21	Once	Slight muco purulent	6th day	Mild whooping cough	1 yr. later typical mod. severe pertussis cough plate +

N. F. 7/38	10 yr.	M	Whoop. cough at 3 yr. W.B.C. = 37,600 67% lymph. Treated with vaccine	Familial exposure to sister G. F. (see below) for 9 days ā onset	Mild paroxysmal night only	—	7	—	—	3rd day	Tracheitis	Negative
G. F. 6/38	7 yr.	F	Whoop. cough at 3 mo. Brother had lymphocytosis (see above) Treat. c̄ vaccine	None known	Mild paroxysmal night only	—	14	—	—	7th day	Tracheitis	Negative
W. W. 6/39	2½ yr.	M	*H. pertussis* vaccine 80 billion 20 mo. previously	Indoors for 8 hours, 8 days ā onset	Nonparoxysmal	—	5	—	Profuse mucopurulent	4th day	Upper respiratory infection	Negative
P. S. 6/39	5½ yr.	F	*H. pertussis* vaccine 80 billion 4 mo. previously	Familial exposure to sister H. S. (see above) for 6 days ā onset	Nonparoxysmal	—	17	—	—	10th day	Tracheitis	1 yr. later familial exposure to pertussis in sister H. S. (see above). Escaped entirely
D. R. 7/40	23 mo.	M	*H. pertussis* vaccine 20 billion cells only given 17 mo. previously	None known	Paroxysmal severe	+	27	Several times	Mucopurulent	4th day	Whooping cough W.B.C. = 10,600 36% lymph.	Negative

*1 c.c. of *H. pertussis* vaccine (20 billion cells) was given elsewhere on the 6th day of cough.

suspension of *H. pertussis*, but parapertussis agglutinins in the serum of a rabbit which has been injected with *H. pertussis* are well absorbed by a suspension of *H. pertussis*).

Bradford and Wold[4] produced interstitial pneumonia in mice by intratracheal or intranasal inoculation with *B. parapertussis*. The pneumonia was often fatal. Survivors were immune. The lesion here was essentially the same as that produced by *H. pertussis* and several unrelated organisms and was not considered a specific type of reaction.

Bruckner and Evans[5] studied the endotoxin of *B. parapertussis* and compared it to those of *H. pertussis* and *Br. bronchiseptica*. These three toxins were found to be similar though that of *B. parapertussis* was not so potent. All were extremely thermolabile. In a later paper Evans[6] was able to neutralize parapertussis toxin with an antitoxin produced with formolized *H. pertussis* toxin.

During the course of routine cough plate examinations for pertussis, we have occasionally isolated *B. parapertussis*. Two strains were isolated in Copenhagen in 1933 though at the time they were not recognized as such. Because of their green cast on Bordet-Gengou medium containing 33 per cent horse blood they were called "Green Strains." Krarup[7] employed them for skin tests. He found that suspensions and autolysates of both *H. pertussis* and "green strains" produced local hyperemia in children regardless of whether or not they had had pertussis. Two additional strains were isolated in 1934. Eldering kindly examined one of them and found that it fulfilled her criteria for *B. parapertussis*.

Our present report describes clinical and immunologic aspects of infection with *B. parapertussis*. Ten cases have been observed at the Stanford University Children's Clinic in the past four years. The organism has been identified by cultural and serologic means. The ten strains isolated were serologically homogeneous.

Table I summarizes the clinical records of our ten cases. Note that five cases occurred in children who had previously had neither *H. pertussis* vaccine nor pertussis. In two of these pertussis developed later. Two cases occurred in children with a positive history of whooping cough, and three occurred in children who had had *H. pertussis* vaccine.

The five cases which occurred in children or infants with negative histories varied widely in severity. Only one (G. N.) presented the clinical picture of whooping cough, i.e., severe paroxysms with whooping and vomiting, and lymphocytosis. The other four cases were decidedly milder. Whooping did not occur, and vomiting was either absent or occurred once or twice. It will be recalled that Bradford and Slavin[3] described moderately severe whooping cough in only two of their eight patients.

In two patients, S. R. and H. S., attacks of pertussis were observed subsequent to the parapertussis. The pertussis occurred seven months

and one year, respectively, after the parapertussis. Though the parapertussis in both patients was decidedly benign, their subsequent attacks of pertussis were not. Repeated whooping and vomiting occurred and persisted for several weeks. The clinical picture was unmistakably that of whooping cough and was confirmed by cough plate or blood count. Certainly no cross protection was evident.

The two cases that occurred in children who had had "whooping cough" previously (N. F. and G. F.) were in a brother and sister. This diagnosis had been made in our clinic seven years previously on the basis of typical clinical findings. A blood count done on N. F. showed lymphocytosis. Both children were treated with small amounts of stock strain *H. pertussis* vaccine without improvement. In retrospect one cannot be sure whether this "whooping cough" was pertussis or parapertussis though the former seems more likely. Their attacks of parapertussis which we witnessed (Table I) simulated tracheitis. N. F. coughed for seven nights, and his younger sister G. F. coughed for fourteen nights; but no typical paroxysms or day coughing occurred. It is possible, of course, that their earlier "whooping cough" modified their course of parapertussis. However, we are inclined to doubt such modification from our observation that parapertussis may be very mild.

The three remaining cases occurred in children who had received *H. pertussis* Phase I vaccine.* Table I gives the pertinent data. Although it may be only coincidental, it is of some interest to note that the two children, W. W. and P. S., who had received the full prophylactic dose of vaccine (80 billion cells) had mild attacks of parapertussis. On the other hand, in D. R., who received only 20 billion cells of *H. pertussis* vaccine, the parapertussis simulated whooping cough and was complicated by otitis media. The possibility is suggested that the vaccine in full dosage may have exerted some cross protection against parapertussis. We know that this vaccine is capable of producing a high degree of specific immunity to pertussis. P. S., a vaccinated child, contracted parapertussis from her sister, H. S., but escaped pertussis completely when the latter was attacked (Table I).

The incubation period of parapertussis is not known. In three instances in our small group of cases a little evidence was obtained. One child (W. W.) had a history of "being exposed to whooping cough indoors for eight hours" twelve days before the onset of his parapertussis. The "whooping cough" had been diagnosed by a physician on clinical grounds and was said to be rather mild. In the "F" family N. F. began to cough fifteen days after his sister, G. F. In the "S" family P. S. began to cough six days after her sister, H. S. A common source of infection for each pair of these siblings cannot be excluded. It would seem likely, however, that N. F. contracted parapertussis from

*Kindly supplied by the Cutter Laboratories.

G. F. after an incubation period of not more than fifteen days. On the other hand P. S. and H. S. may have been infected from a third common source.

IMMUNOLOGIC STUDIES

The appearance of *H. pertussis* agglutinin after vaccination with Phase I *H. pertussis* vaccine and after attacks of pertussis has been reported by many workers. With the technique that we have used,[8] pertussis agglutinin, usually in high titer, has been found to persist for more than four years after the administration of Phase I vaccine. On the other hand, the agglutinin response to an attack of pertussis was found to be highly variable. In a few persons no agglutinins were demonstrable, and in others a comparatively low titer which often disappeared within eighteen months was attained.[8] When the same technique has been used, the development of agglutinins against *B. parapertussis* has been observed.

Table II indicates the agglutinative titers obtained in the ten cases of parapertussis studied. These data indicate that parapertussis regularly results in the production of specific agglutinins which may appear as early as twelve days after the onset (H. G.).* The agglutinins may persist in high titer for twenty-seven months after the attack (G. G.) and in lower titer for a longer period (S. R.).

If the agglutinative reactions in those persons with negative histories are examined, it appears that the response to an attack of parapertussis is specific. No cross reaction, indicated by the presence of pertussis agglutinins, could be demonstrated in the sera of G. G. or H. G. The patient G. N. was given *H. pertussis* vaccine elsewhere with therapeutic intent before he came to us. His serum showed a low titer of pertussis agglutinins on the eighteenth day, but it subsequently became negative while specific parapertussis agglutinins appeared. The patient H. S. showed specific agglutinins five days after her parapertussis (and failed to develop *H. pertussis* agglutinins one year later when she had pertussis). This absence of cross reacting antibody in the serum of convalescents from parapertussis is of interest. Rabbits injected with *B. parapertussis* usually produce a serum that contains *H. pertussis* agglutinins as well.[2, 3, 5]

Infections with *B. parapertussis* appear to be more regularly followed by the appearance and maintenance of serum agglutinins than do infections with *H. pertussis*. In this connection, examination of sera from children who had both infections is pertinent. It will be noted that, whereas H. S. carried a high titer of *B. parapertussis* agglutinins for twenty-six months after her infection with this organism, she failed to develop *H. pertussis* agglutinins after her pertussis. Furthermore, in

*The parapertussis agglutinins demonstrated on the fourth day of the attack in the case of W. W. may or may not be a specific response to the infection since W. W. had *H. pertussis* vaccine.

S. R., N. F., and G. F. the titer of *H. pertussis* agglutinins was lower than that of the *B. parapertussis* agglutinins.

As mentioned above the specific agglutinin response to *H. pertussis* vaccine is usually high and prolonged when 80 billion cells are given.[8] Table II indicates that W. W. had a titer of 1:1,280 eighteen months after vaccination. This titer remained essentially the same throughout his attack of parapertussis and persisted for one year thereafter. P. S., on the other hand, had a low titer, 1:80, before the onset of her parapertussis. After the attack the titer was higher—probably a nonspecific stimulation. D. R., who had been given only a small amount of *H. pertussis* vaccine, was known to have had little or no pertussis antibody and no parapertussis antibody before his attack. Seven months afterward his serum agglutinated *B. parapertussis* 1:1,280 but failed to agglutinate *H. pertussis*.

In view of the fact that the symptoms of *B. parapertussis* infection in six of our ten cases (Table I) were not typical of whooping cough, it is reasonable to suppose that infection with this organism may be quite common. It is quite obvious that bacteriologic tests are not and cannot be made in every instance of tracheitis and upper respiratory infection. We isolated this organism simply because we were interested in pertussis. If the formation of *B. parapertussis* agglutinins occurs with regularity during and after an attack and if the antibodies persist as long as we have found them to, missed cases might be detected by this reaction.

With this in mind the sera of fifty children with negative histories for pertussis and *H. pertussis* vaccine were examined with both antigens. Twenty sera (40 per cent) contained *B. parapertussis* agglutinins, usually in titers above 1:80, whereas seven sera (14 per cent) contained *H. pertussis* agglutinins, usually in lower titers (Table III). This finding suggests that *B. parapertussis* infections, with or without symptoms, are common in this community. The increasing incidence of positive sera with increasing age is also compatible with this hypothesis.

Although the incidence of sera positive for *H. pertussis* (14 per cent) is less than that of sera positive for *B. parapertussis* (40 per cent), it can hardly be concluded that undiagnosed *H. pertussis* infections are less frequent. As noted above, the appearance of specific agglutinins in pertussis is irregular and the duration of their carriage is limited. Therefore, a comparison of the incidence of agglutinins for these two organisms cannot serve as a reliable index of the extent of infection with them.

It is perhaps pertinent to note in Table III that all sera positive for *H. pertussis* were also positive for *B. parapertussis* and that no serum was positive for *H. pertussis* alone. This suggested the possibility that infection with *H. pertussis* might lead to the production of cross reacting parapertussis antibody. Sera were therefore obtained from twenty-

TABLE II

AGGLUTINATIVE REACTIONS

CASE	HISTORY	BEFORE ATTACK OF PARAPERTUSSIS			DURING ATTACK OF PARAPERTUSSIS			AFTER ATTACK OF PARAPERTUSSIS		
		TIME	TITER VS.		TIME	TITER VS.		TIME	TITER VS.	
			B. PARAPERTUSSIS	H. PERTUSSIS		B. PARAPERTUSSIS	H. PERTUSSIS		B. PARAPERTUSSIS	H. PERTUSSIS
G. G.	—							10 mo. 15 mo. 21 mo. 27 mo.	1:1280 1:640 1:640 1:640	Not done 0 0 0
H. G.	—				7th day 12th day	0 1:160	Not done 0			
G. N.	—*				18th day 28th day 34th day	0 1:160 1:320	1:80 0 0	5 mo.	1:160	0
S. R.	Past history negative							24 m. p para. 17 m. p pert.	1:80	1:20
	7 mo. p paratussis had typical whooping cough with lymphocytosis							29 m. p para. 22 m. p pert.	1:160	0
								34 m. p para. 27 m. p pert.	1:40	0
								40 m. p para. 33 m. p pert.	1:20	0

H. S.	Past history negative				10th day	0	0	5 days	1:80	0
								4 mo.	1:160	0
								9 mo.	1:640	0
	1 yr. p̄ parapertussis had moderately severe pertussis with + cough plate							12 m. p̄ para. 2nd d. of pert.	1:320	Not done
								13 m. p̄ para. 40th d. of pert.	1:640	0
								17 m. p̄ para. 4 m. p̄ pert.	Not done	0
N. F.	Whooping cough 7 yr. previously. Treated with vaccine then							21 mo.	1:160	1:40
								26 mo.	1:320	1:20
G. F.	Whooping cough 7 yr. previously. Treated with vaccine then							21 mo.	1:80	1:20
								28 mo.	1:160	1:40
W. W.	*H. pertussis* vaccine 80 billion cells 20 mo. previously	18 mo. after vaccine and 2 mo. before parapertussis	Not done	1:1280	4th day 11th day	1:40 1:320	1:640 1:640	3 mo.	1:640	1:1280
								8 mo.	1:640	1:1280
								12 mo.	1:1280	1:1280
P. S.	*H. pertussis* vaccine 80 billion cells 4 mo. previously	4 mo. after vaccine and 1 day before onset of parapertussis	Not done	1:80				3 days	1:160	1:320
								4 mo.	1:160	1:160
								9 mo.	1:320	1:320
								13 mo.	Not done	1:320 †
D. R.	*H. pertussis* vaccine 20 billion cells only, 17 mo. previously	15 mo. p̄ vaccine 2 mo. ā para	0	0				7 mo.	1:1280	0
		17 mo. p̄ vaccine 1 day ā para	0	1:10						

*1 c.c. of *H. pertussis* vaccine (20 billion cells) was given elsewhere on the 6th day of cough.
†At this time exposed to pertussis in sister and escaped.

TABLE III

AGGLUTINATION REACTIONS IN 50 CHILDREN WITH NEGATIVE HISTORIES

AGE IN YEARS	< 1			1-3			3-5			5-7			7-9			9-11			11-15			ALL AGES
NUMBER (#) OF SERA AND THEIR TITER	(#)	PARA	PER	(#)	PARA	PER	(#)	PARA	PER	(#)	PARA	PER	(#)	PARA	PER	(#)	PARA	PER	(#)	PARA	PER	(#)
Sera containing only parapertussis agglutinins	1	160	0	0			2	640 160	0 0	4	160 640 20 40	0 0 0 0	2	640 80	0 0	1	160	0	3	640 20 640	0 0 0	13
Sera containing only pertussis agglutinins	0			0			0			0			0			0			0			0
Sera containing both agglutinins	0			0			1	2,560	10	0			2	1,280 320	20 20	2	320 640	640 160	2	160 160	10 160	7
Sera containing no agglutinins	12			6			8			2			1			1			0			30
Total number sera tested	13			6			11			6			5			4			5			50
Total number sera positive for parapertussis	1			0			3			4			4			3			5			20 40%
Total number sera positive for pertussis	0			0			1			0			2			2			2			7 14%

Para = parapertussis agglutination titer; per = pertussis agglutination titer.

two children during an attack of pertussis, all proved bacteriologically. In only one instance was parapertussis agglutinin observed to appear. It was preceded by the appearance of specific pertussis agglutinin, and it disappeared while the latter persisted. This finding indicates that only very occasionally an attack of pertussis may give rise to transient cross reacting antibody. As we noted above, an attack of parapertussis has not been observed to give the reverse cross reaction.

The question of whether *H. pertussis* vaccine in the usual dosage gives rise to the production of nonspecific *B. parapertussis* agglutinins in children was examined. Eleven children with negative histories and with negative agglutinative reactions for both *B. parapertussis* and *H. pertussis* were given 80 billion Phase I *H. pertussis*. Sera were obtained one to nine months later. All sera contained *H. pertussis* agglutinins in the usual range of 1:160 to 1:1,280, and two sera contained *B. parapertussis* agglutinins in dilutions of 1:10 and 1:20. This indicates that nonspecific parapertussis antibody is occasionally produced in children by the usual doses of *H. pertussis* vaccine. Corroborative of this conclusion is the evidence cited in Table IV. There it is seen that, in the sera of 51 per cent of eighty vaccinated children, *B. parapertussis* agglutinins were present. This percentage of parapertussis reactors is only slightly greater than that found in the group of children with negative histories, 40 per cent (Table III). The difference is statistically insignificant (11 per cent ± 8.9 per cent).

TABLE IV

AGGLUTINATIVE REACTIONS IN CHILDREN WHO HAD RECEIVED H. PERTUSSIS VACCINE

Positive for both { *H. pertussis* / *B. parapertussis* }	41	51%
Positive for *H. pertussis* only	35	44%
Positive for *B. parapertussis* only	0	0%
Negative for both	4	5%
Total	80	100%

In addition to the agglutination reactions described, the mouse protection test was used to study the formation of antibodies against parapertussis in a few instances. The technique used will be described elsewhere.[9] It was observed that mouse protective substances were not present in the serum of the patient G. N. on the eighteenth day of his attack of parapertussis. Serum obtained on the twenty-eighth day however protected eight of ten mice, and serum obtained on the thirty-fourth day protected ten of ten. Serum obtained five months after the onset likewise protected all of ten mice. The sera of W. W. and G. G., who had parapertussis one and two years previously, were protective, whereas that of S. R., who had parapertussis more than three years previously, did not protect any of ten mice injected.

SUMMARY

Ten cases of respiratory infections in children due to *B. parapertussis* are described. Only two presented the classical picture of whooping cough, and in two more the clinical diagnosis was mild whooping cough. The remainder presented the symptoms of tracheitis or upper respiratory infection.

Two of the children had had whooping cough previously, and three had had *H. pertussis* vaccine. In two other children typical pertussis occurred seven months and one year, respectively, after the attack of parapertussis. Thus apparently cross protection does not occur.

In three instances where exposure was known the incubation periods were six, twelve, and fifteen days. In the case of the child whose onset of parapertussis was six days after that of her sister an earlier exposure common to both siblings seems likely.

The appearance of specific agglutinins was demonstrated in all of the ten cases. The agglutinins persisted for as long as forty months. Nonspecific *H. pertussis* agglutinins did not appear and were found only in the sera of those children who had also had pertussis or *H. pertussis* vaccine.

B. parapertussis agglutinins were also found in 40 per cent of the children with negative histories for parapertussis, pertussis, and *H. pertussis* vaccine. This suggested that the incidence of unapparent *B. parapertussis* infections in this community is relatively high.

It was observed that attacks of pertussis and injections of *H. pertussis* Phase I vaccine may very occasionally give rise to the production of nonspecific parapertussis antibody in low titer.

The development of specific mouse protective antibody in the sera of three patients with parapertussis was observed.

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NUTRITIONAL OBESITY IN CHILDREN IN PRIVATE PRACTICE

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IN ORDER to be particularly definite, it is to be understood that the children comprising the group were not ill; in fact, as a rule they were unusually well, carrying on in a normal fashion in the home and school. Neither would they be considered habitually indolent, so-called lazy children. They were quite normal in fact, except for the obesity which was the reason for the consultation. With few exceptions they were members of well-to-do or privileged families.

The combined weight of these 168 obese children was 17,553¾ pounds, averaging 37¼ pounds of excess weight for each child, and representing 6,243½ pounds of overweight for age.

Each patient was given a complete physical assessment to determine possible physical agencies in producing the overweight. This examination included height, weight, posture, orthopedic aspects, the buccal cavity, the teeth, tonsils, ears, and nasal passages, x-ray of the accessory sinuses in many, and the condition of the heart, lungs, liver, spleen, abdomen, genitals, skin, blood, urine, and blood pressure in each patient, basal metabolic rate when possible, and bone age assessment invariably.

At the completion of the examination it was explained to the family that the child was free from organic illness, that the excessive overweight according to our findings was due to dietary indiscretions, and that the management related chiefly to the nature and the amount of the food intake.

It was emphasized that if cooperation as related to food habits was not worth the effort, it was useless to attempt treatment. Our report as to normality, the assurance that the child was not ill, particularly that the condition was not one of an endocrine nature, explains why forty-nine failed to return for further observation.

Not a few of the parents expressed disappointment that gland therapy was not to be part of the treatment. Nineteen additional cases were dropped because of failure to continue the dietetic plan. One hundred and three constituted the group who carried out the diet schedule given in Table II.

The administration of vitamins A, B, and D in generous amounts supplemented the feeding plan to compensate for the reduced vitamin A and D in the diet. It is shown that a diet schedule may be arranged, keeping in mind nutritional and calorie values, that will not only prevent further increase in overweight but act as a means in its reduction without harm to the individual.

TABLE I

CHILDREN IN FAMILY		SEX		RELIGION	AGE	
1 child	44	Female	95	79 Christian	Under 5 years	7
2 children	83	Male	73	89 Hebrew	5 to 10 years	70
3 children or more	41				10 to 15 years	84
					15 and 16 years	7

TABLE II

		CARBOHYDRATE	PROTEIN	FAT
Fruits	All cooked and raw fruits except banana, ½ cup or 4 ounces	14.4	0.7	
Fruit juices	Tomato, orange, or grapefruit, 1 cup or 8 ounces	18		
Eggs	Boiled, poached, or scrambled egg without fat, 1		7.7	6.9
Cheese	Any variety, 2 ounces	1	13.3	18.1
Meats	Poultry, lamb, beef, liver, or fish, 3 to 4 ounces		27	5.4
Vegetables	Spinach, lettuce, celery, tomatoes, string beans, cabbage, brussel sprouts, chard, cauliflower, broccoli, onion, asparagus, ½ cup at each of two meals	8	2	
Salads	Any of above vegetables or fruit served with lemon and mineral oil dressing, ½ cup at each of 2 meals	8	2	
Desserts	Fruit, gelatin, sherbets, skim milk puddings, ½ cup at one meal	30	3.6	0.4
Breads	Preferably whole-wheat or rye, ½ slice at each meal; Ry-krisp	21	4.5	1.8
Beverages	Skim milk, not over 1 pint daily; cocoa made with skim milk; saccharine to be used as sugar, ¼ gr. tablet equalling 1 teaspoon sugar	25	17.4	1
Total calories, 1115.8		125.4	78.2	33.6
Approximately 1000 to 1200 calorie diet		125	75	35

SAMPLE MENU

BREAKFAST	DINNER OR LUNCH	LUNCH OR DINNER
1 cup orange juice	3 to 4 oz. lean meat or fish	Cottage cheese on lettuce, 2 oz.
1 egg	½ cup cooked spinach	Asparagus salad, ½ cup
1 glass skim milk	½ cup orange and grapefruit	½ cup string beans
½ slice whole-wheat bread	Salad on leaf of lettuce	½ slice bread
	Mineral oil mayonnaise	1 glass skim milk
	½ slice bread	½ cup frosted raspberries
	1 glass skim milk	
	Lemon sherbet	

The only therapeutic measure employed in this study relates particularly to the amount and nature of the food intake together with suggestions as to the necessity of carrying on the physical activity peculiar to children.

These children were very much alike regardless of nativity, age, or sex. Nutritionally obese children present a similarity in the physical and psychic that establishes a definite entity.

In addition to overweight for age, overheight for age, and overweight for height, their mental endowment is superior or equal to children of the same age free from a constitutional dyserasia.

Their dispositions as evidenced in the home, in the school, and in social contacts are usually of a satisfactory average for children of the same age.

Alike are they in possessing habitually insatiable appetites and a capacity for excessive food intake without resulting illness.

Again, they are alike in their complete absence of dependability relating to food restrictions and their preference for sweet and starchy foods.

Indolence and mental inferiority in the obese child strongly suggests that additional pathogenic factors of an organic or developmental nature are present and are to be searched for. These organic cases exhibit markedly different symptoms from those of the nutritionally obese child.

The results in this group of 103 patients who conscientiously followed out the diet plan suggested are shown in Table III.

TABLE III

AGE LAST BIRTHDAY (YR.)	NO. OF CASES	OVERWEIGHT FOR AGE* (POUNDS)	OVERWEIGHT FOR HEIGHT* (POUNDS)	LOSS IN WEIGHT* (POUNDS)	INTERVAL* (WK.)
2	1	16	16	4	6
4	3	22½	18½	3	11
5	2	25	21	3	3
6	4	29½	21¾	4½	6
7	13	43	31½	3¾	6
8	7	41½	36¼	5	12
9	9	36¾	29	5¼	10
10	19	35¼	29½	7½	11
11	8	43	30	11½	8
12	14	48½	37¾	11	7
13	8	53¼	48½	13¾	16
14	8	49¼	32¾	11¼	13
15	3	78	58	13	7
16	4	44½	34¼	13½	14

*Indicates average.

In the application of the diet plan, reasonable latitude is permitted, particularly in the older patients. This will be found necessary in order to secure continued cooperation over considerable periods constituting a re-education of the eating habits.

At all ages one or two apples a day may be eaten at any time. Occasionally additional portions of meat, fish, or eggs may be given for the sake of variety.

A portion of cooked cereal may be added to the breakfast of the older children if desired.

It will be seen that the addition of these foods will add very little to the calorie content of the food ingested, keeping it well under 1,500, which means at least a 50 per cent reduction in the previous eating habits.

The results in five outstanding cases among the older children demonstrate the advisability of catering a bit to dietetic adjustment. A male, aged 15 years, lost 30 pounds in three months; female, aged 14½ years, lost 30 pounds in four months; male, aged 11 years, lost 27 pounds in three months; female, aged 10 years, lost 26½ pounds in ten months; male, aged 12 years, lost 23 pounds in three months.

The study presented covers the dietetic management of 103 cases of nutritional obesity. Weight increase was not only retarded, but weight loss was made by each child. Our results demonstrate that in purely nutritional cases of obesity in children, weight loss will result if the plan suggested is carried out.

In the preparation of this contribution we acknowledge our indebtedness to Beatrice Donaldson, dietetitian; to Emma Godfrey, technician; and to Dr. Hilde Bruch and Alice Kelly for their arrangement of the text and charts.

RESTRAINT FOR SMALL CHILDREN

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THE problem of preventing accidents to children in the hospital ward is an ever present one. The small infant rarely falls out of bed, but as soon as he can struggle to his feet, or even to his knees, the baby is likely to tumble out of bed if the side is low. The runabout will climb out of a high-sided crib. The result may be no more than a bumped head, but it may be a broken clavicle or arm bone, or even a skull fracture. The old hospital bed with a side only a few inches above the mattress was a constant menace to the larger infant. The runabout had to be restrained or he would surely fall out, even if he had made no deliberate effort to climb out.

In attacking this problem, the first thought was a better hospital bed. In 1928 and 1929, when the equipment for the new Babies' Hospital in New York City was ordered, the problem of the hospital bed for children was recognized as one which had never been solved. At that time the standard infants' beds were of the type shown in Figs. 1, 2, and 6. The sides were fixed. The springs could be raised or lowered, but when in the low position, the bed was hard to make and the patient too low for easy access for nursing and examination. To raise the bed required two persons, and strong ones at that. Even in the low position the sides were only a few inches above the mattress and many children fell over them.

The new style beds (Fig. 5) were first made by the Frank Hall Co. on the specification suggested by me, after a study of the beds on the market at that time and consultation with the nurses of Bellevue and Presbyterian Hospitals. The mechanical part of the design was entirely the work of the makers. These beds were soon copied by many manufacturers who use slightly different mechanical plans, but the principles involved are the same. This type has now supplanted the older bed in many hospitals.

The specifications on which these beds were designed were as follows:

1. The sides must be as high as possible above the mattress level to minimize the dangers of accident.

2. The mattress level must be fixed at a convenient height for nursing and examination (34 inches).

3. Both sides must be easily lowered, and the device for locking must work quickly and without the use of both hands. A foot pedal is used on the best beds.

4. When lowered, the upper rail of the side must be below mattress height to facilitate bed making.

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The height to which the side can be raised is determined by the mattress level, because it is not feasible to raise the fixed height of the spring

Fig. 1.

Fig. 2.

Fig. 1.—Child in restraint jacket in old type bed. The sides of the bed were so low that any baby able to sit up might fall out, and some form of restraint was necessary. The muslin jacket is fastened around the trunk of the child and has four strong bands of cloth which are attached to crib rods. It is not difficult for a determined, struggling baby to become entangled in the bands. Babies have been strangled in this form of restraint, even when the upper pair of bands were fastened transversely to the crib rods, instead of obliquely as in this photograph.

Fig. 2.—Child sitting up in bed with only two bands fastened to crib. It is possible for him to twist himself beneath the bands.

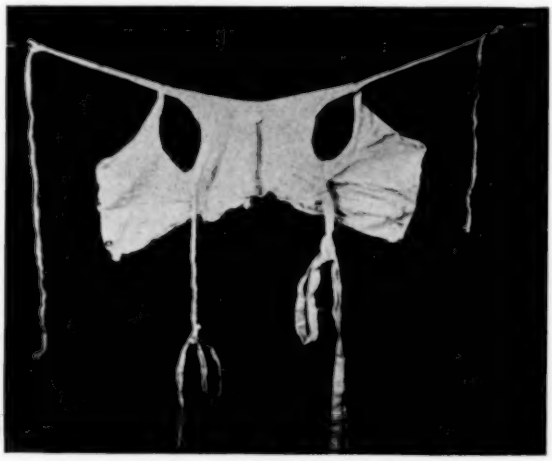

Fig. 3.—Jacket of muslin, with bands, the standard restraint method formerly used. The lower bands are shortened with loops merely to get them all into the photograph.

and mattress above a convenient point. Therefore, the maximum height of the side of most of these beds above the mattress is about 21 inches.

These beds are safe for infants, but the active and acrobatic runabout will climb up and fall over the side of almost any crib. To meet this difficulty, various forms of restraint have been used. The one shown in

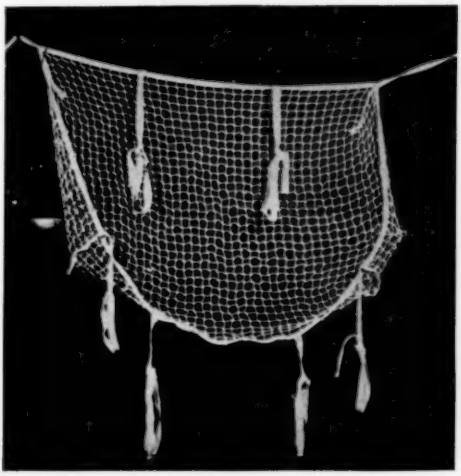

Fig. 4.—Fish net cover for bed. Note that the shape of the net is distorted by hanging against the wall. The box corners may be seen at the bottom but are not well shown at the top on account of position. The bands are looped to shorten them in order to make the photograph more compact. They are actually long and straight.

Fig. 5.—Child in new type bed with new fish net cover. The sides are 21 inches above mattress level, but an active child can climb over them. Fish net makes a cage within which the patient can tumble about freely. Note that the bands are tied to the legs of the crib with bow knots, out of the child's reach.

Figs. 1, 2, and 3 is a common example of this type, a jacket or bands around the trunk, with tapes or bands to fasten to the bed rods or under the mattress. These bands constitute serious danger to the baby. The active child who resents restraint twists and tosses and may work himself into a position in which he can get his head and neck under the bands. Several accidents have happened in which the child has wound himself up in an incredibly short time, almost under the nurse's eye. At least three deaths have come to my knowledge in different hospitals from this cause.

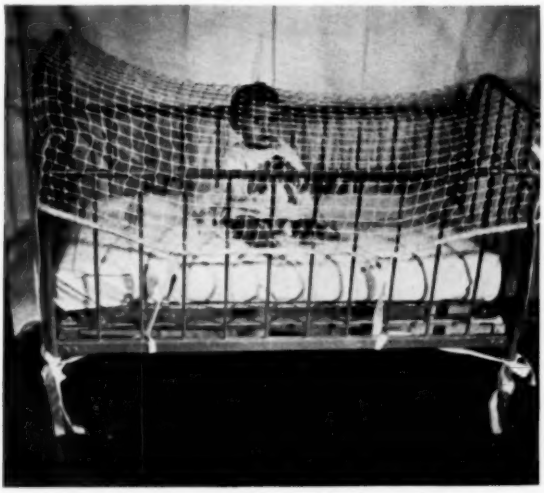

Fig. 6.—Fish net cover over old type bed with low sides. Child can sit up but cannot stand.

After an accident with this form of restraint, a new plan was tried. It was so successful that it has been adopted in all New York City hospitals as a standard restraint for small children. It is merely a heavy fish net tied over the top of the crib, making what amounts to a small cage. (Figs. 4, 5, and 6.) The child is free to tumble about in it, to sit up, and to stand if he is not too tall. The net must be large enough to come well down over the crib sides and ends so that the child cannot get his head between the edge of the net and the bed. It must be fastened securely, yet it must be possible to remove it quickly. Heavy webbing is sewn along the borders of the net, and this binding is extended to form tapes long enough to tie to the legs of the bed. Bow knots are used on one side at least. The nurse can quickly untie the tapes with a pull and raise the net or lower the side of the crib enough to get at the child in a few seconds.

This plan is reported in the hope that it may help other hospitals to prevent accidents. A bumped head or a broken clavicle is humiliating, but a death from choking is a tragedy.

Critical Review

TREATMENT OF HEMOLYTIC STREPTOCOCCAL INFECTIONS

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IT IS no longer necessary to call attention to the dramatic results which sulfanilamide has brought about in certain beta hemolytic streptococcus diseases in the three and one-half years since a symposium[1] dealing with the early use of the drug was published in the Journal of Pediatrics. Until the advent of effective chemotherapy, hemolytic streptococcal infections in which there was invasion of the blood, the meninges, the peritoneum, or the lungs, and erysipelas of the newborn infant, carried a fatality rate of from 60 to 100 per cent. In these highly fatal conditions, sulfanilamide has brought about such a striking change that the results constitute practically rigid experimental proof of its effectiveness. The question now is whether the limits of its usefulness can be defined: to what extent is there clinical or experimental evidence of its effectiveness in the milder infections, and, particularly, in prophylaxis.

Of the various sulfonamide derivatives, it is generally agreed that in streptococcal infection, sulfanilamide is preferable because it is better absorbed and shows less tendency to acetylation.[2*] Since the appearance of Domagk's paper in 1935,[3] the literature pertaining to sulfanilamide and its derivatives has become vast. It has been most helpful, therefore, to have available the reviews by Marshall,[4] Bigler and Haralambie,[5] Kolmer,[6] and the newly published pharmacology text by Goodman and Gilman,[7] of the Yale Medical School. Since therapeutics must have its basis in pharmacology if it is not to be empirical, it might be well to review briefly the pharmacology of sulfanilamide.

MECHANISM OF ACTION

The precise mode of action of this drug is still undetermined. Lockwood[8] believes that sulfanilamide prevents utilization by the bacteria of a protein substrate essential for their growth.† The view of Mellon and his associates[9] is that the oxidative action of the bacteria produces a substance from sulfanilamide that has anticatalase activity; as a result, hydrogen peroxide accumulates in such quantity as to be bacteriostatic, whereas normally the hydrogen peroxide formed by bacteria in the course of their metabolism is removed by the catalase present in the blood and tissues. A third theory advanced by Mayer and extended by Shaffer[10, 11] and also by Fox[12] is that sulfanilamide is oxidized in the body to parahydroxylaminobenzenesulfonamide, which produces the therapeutic effect as well as the methemoglobin. While there is consider-

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*Sulfadiazine, not yet official, is under clinical investigation and may prove equal or even superior to sulfanilamide (Bull. Johns Hopkins Hosp. 67: 427, 1940.)

†It is held that p-aminobenzoic acid is the probable natural antisulfanilamide factor essential for growth of susceptible bacilli and is normally synthesized by certain bacteria. The enzyme reaction involved in further utilization of this substance is subject to competitive inhibition by sulfanilamide (Marshall, E. K., Jr.: Bacterial Chemotherapy, Ann. Rev. Physiol. 3: 643, 1941.)

able experimental support for each of these views, exceptions have been noted which militate against the complete acceptance of any one view.[11, 13, 13a]

From in vitro experiments it can be concluded that sulfanilamide concentrations of the order attained in the blood and tissues during treatment are definitely bacteriostatic and, under certain conditions, bactericidal. A number of factors have been shown to be operative: the strain of streptococcus, the size of the initial inoculum, the composition of the nutrient medium, the temperature at which the test is performed, and the duration of the experiment.

The action of the drug in vivo against experimental streptococcus infection has been studied chiefly in the mouse. Variable results are attributable to varying procedures and only recently have quantitative methods been developed.[14, 15] The carrying-over of these results from mouse to man has been justified abundantly by clinical experience.

There is general agreement that the drug does not stimulate or affect the defense mechanisms of the host, except secondarily. It acts upon the bacteria, inhibiting their growth, but probably does not produce direct bactericidal effects by the concentrations reached in the tissues with the doses employed clinically. In Longcope's experience,[16] the giving of sulfanilamide over fairly long periods of time did not always eliminate hemolytic streptococci from infected tonsils. Colebrook and Kenny,[17] likewise, noted the failure of the drug to bring about the disappearance of hemolytic streptococci from the lochia of patients convalescing from puerperal infection. Relapses after withdrawal of the drug are explained on the basis that improvement was brought about by bacteriostasis but that the organisms had not been destroyed by the body defense mechanisms and thus reinvasion of the tissues was permitted from a local focus when the medication was stopped. In urinary tract infections, however, sulfanilamide actually may produce sterilization by bactericidal action, when hydrogen-ion concentration and concentration of the drug are optimal. This is due to the fact that in urine, concentrations of sulfanilamide are reached which are ten to twenty times higher than those attained in the blood, and also that urine is a poor medium for bacterial growth. The combination of high concentration and poor environment results in death of the organisms in the urinary tract.

It has been pointed out also that the pathologic character of the infectious lesion may be of as great or greater importance in determining the effectiveness of sulfanilamide than the bacterial species involved.[18] Thus, infections of serous and synovial membranes are generally susceptible to sulfanilamide therapy; on the other hand, localized abscesses of soft tissue or bone and suppurative thrombophlebitis are comparatively resistant. The drug may have some effect in preventing the spread of the infection to adjacent tissues but actually may mask the clinical signs and symptoms of the abscess. Resistance to or inhibition of the bacteriostatic action of sulfanilamide and its derivatives has been noted in both in vitro and in vivo experiments.[19, 20]

ABSORPTION, DISTRIBUTION, AND EXCRETION

Sulfanilamide possesses no pharmacologic action of therapeutic value other than its effects on bacteria. It is absorbed from the small and large intestine within three to five hours, and even in diarrhea the fecal excretion of the drug is negligible. It is rapidly and uniformly distributed

throughout all body fluids in a manner similar to urea. "This rapid diffusion and penetration of the drug to all parts of the organism is undoubtedly one of the factors which make the substance a successful chemotherapeutic agent."[4] It exists in the body fluids in the unchanged or free form and in the conjugated or acetylated form. Individuals vary considerably in the degree to which they conjugate the drug, but as a rule from 10 to 20 (limits, 0 to 40) per cent of the drug exists in the body in the conjugated form. The latter has no therapeutic effect and yet may yield toxic derivatives. The major part of the drug (93 per cent) is excreted in the urine. If the renal function is poor, the drug may accumulate in the body and the retained drug may be progressively acetylated. Water diuresis hastens its excretion and this is very useful in patients manifesting toxic symptoms. Conversely, when it is desired to maintain high levels in the blood, fluids are restricted. The conjugated drug is much less soluble than the free form and may precipitate out from the urine at room temperature.

TOXIC EFFECTS

Therapeutic doses may produce a wide variety of toxic manifestations,[21, 22, 23] most of which are mild and inconsequential, but a few of which are serious and occasionally fatal. They occur as the result of progression of milder toxic effects, excessive dosage, or idiosyncrasy. It is important to recognize them and to differentiate them from the illness for which the drug is administered. Serious effects, such as agranulocytosis, hemolytic anemia, and hepatitis, which require immediate cessation of the drug and active treatment, fortunately are rare and are ascribed to idiosyncrasy, although Watson and Spink[24] regard the anemia and hepatitis as a more marked degree of the usual toxic effect of the drug on the hematopoietic system. The more common but less serious toxic effects are nausea, vomiting, anorexia, cyanosis, mental symptoms, drug fever, rashes, disturbance in acid-base equilibrium, mild granulocytopenia, and anemia. Sulfanilamide does not seem to damage the kidneys directly and, therefore, no special precautions have to be observed in respect to the urine; with sulfapyridine and sulfathiazole, however, the appearance of the freshly voided urine needs to be observed for hematuria, and the total daily output must be measured.

THERAPEUTICS

Therapy with sulfanilamide should be designed to meet the requirements of the individual case. Dosage depends upon the age of the patient, the type and severity of the infection, the route of administration, the functional capacity of the kidneys, and the success with which the desired blood level is attained. Children, as is well known, tolerate the drug better than adults, and 1 to 1½ gr. (0.065 to 0.1 Gm.) per pound in twenty-four hours in four to six doses (maximum, 120 gr., or 8 Gm.) is the usual amount. In severe infections, one-third to one-half of the twenty-four-hour amount is given as an initial dose, and higher daily amounts are used.

For optimal therapeutic results, the desirable blood level in severe infections is from 10 to 15 mg. per cent; for moderately severe infections, 7 to 10; and for mild infections, 4 to 7. Ordinarily sulfanilamide is given orally, either in tablet form or pulverized in sweetened water. To infants it can be given in the formula, and to older children, in cereal or other acceptable soft food. Subcutaneous administration of an 0.8

per cent solution in physiologic saline can be utilized in a comatose or uncooperative patient, in very ill infants, in cases in which there is vomiting, and in cases in which satisfactory blood concentration has not been obtained by the oral route. There is otherwise no advantage in giving the drug subcutaneously. Intravenous injections are unnecessary, but the intravenous drip method has been used.[25] It has been given intrathecally; it may be given by retention enema, but absorption is considerably slower; it has been used topically in surgery.[18b]

It is desirable that patients receiving sulfanilamide have their blood levels determined and blood counts checked at regular intervals, but as Long[26] points out, careful clinical observation alone should disclose most of the toxic reactions fairly early.

The main contraindication to sulfanilamide is the history of previous serious toxic reactions, such as agranulocytosis, acute hemolytic anemia, purpura, drug fever, jaundice, or severe dermatitis. With such a history, it is best to give a small test dose of the drug orally (0.1 to 0.3 Gm.) and then to observe the patient for acute toxic manifestations over a period of twelve hours before vigilantly beginning the course of therapy.

The routine use of alkali seems now an added and unnecessary burden to a sick patient; when the proper intake of salt is assured, adequate renal function regulates the electrolyte pattern and the acid-base balance of the body. Cyanosis, due to the formation of methemoglobin (rarely sulphemoglobin), can be controlled with methylene blue given orally. The necessity for relieving cyanosis may arise in patients having a low hemoglobin, in patients in whom general anesthesia is contemplated, or in patients in whom cyanosis from causes other than sulfanilamide has to be differentiated; the slow intravenous injection of a 1 per cent aqueous solution of methylene blue in a dose of 1 to 1.5 mg. per kilogram is said to bring relief in thirty minutes.[11] Transfusion is indicated if the hemoglobin drops to 50 or 60 per cent. While sulfanilamide persists in the tissues, the patient should not be exposed to sunlight or ultraviolet irradiation. Other drugs may be employed safely concurrently with sulfanilamide, and it is not necessary to forbid sedative doses of barbiturates. The forcing of fluids may militate against obtaining the desired blood level, but the fluid intake should be adequate to maintain a satisfactory urinary output.

It usually has been said that no special diet is indicated or contraindicated. Early this year, however, there was published a report[27] from the National Institute of Health indicating that the toxicity of sulfanilamide in rats is influenced by dietary protein, a liberal intake preventing excessive blood destruction following prolonged treatment with sulfanilamide. This work was suggested by previous experiments[28] showing that the chronic toxicity of selenium could be mitigated or completely prevented by the inclusion of liberal protein in the diet. Studies from Whipple's laboratory at Rochester[29, 30] show that chloroform liver injury increases as protein stores decrease and that arsphenamine liver injury can be modified by a high protein diet. The benefit from infusion of glucose solution may be due to its sparing effect on protein, for even greater effects accrue from more liberal protein intake. If these experimental results are found to obtain in clinical studies, an important step will have been taken in mitigating the rare but serious toxic reactions from therapy with sulfanilamide. It would appear,

therefore, that a high protein, high carbohydrate, low fat diet is desirable.

Adjuvant measures should not be forgotten, for patients are still encountered who prove irresponsive to chemotherapy or in whom metastatic foci develop during the course of treatment, as reported by Botsford and Lanman[31] and others. It is necessary, therefore, to emphasize that chemotherapy does not obviate surgical drainage when indicated, or the employment of serum or symptomatic treatment. Although it is recognized that when chemotherapy alone is effective, little harm results from the failure to administer serum, there are situations in which the use of antistreptococcus or convalescent serum may add to the probability of cure by the addition of antibodies.[32, 33] In highly toxic scarlet fever, for example, serum brings about so sharp an amelioration of the prostration and toxemia that it should be used even if sulfanilamide is thought to be indicated. Experimental work[34-36] has tended to show the value of combining serum and sulfonamide drug therapy, although the clinical evidence is not conclusive.[26]

Let us compare now the therapeutic use of sulfanilamide in the two beta hemolytic streptococcus diseases, erysipelas and scarlet fever. In the former, as has been mentioned, it has proved satisfactory and has entirely changed the management of the disease.[37-39] Its value in the routine treatment of scarlet fever, on the other hand, is not established. A recent report by Rascoff and Nussbaum[40] gives the results of a controlled study and reviews much of the literature, but the work of Bozalis and Barnett[41] and our own,[42] both published in April, 1940, are not included. Practically all the carefully controlled studies, including our own, fail to show decided and impressive effects of sulfanilamide in preventing complications of scarlet fever. Uncontrolled studies in a disease so variable and so prevailingly mild must not be given undue consideration. It is not out of place to recall the general use of convalescent serum in early poliomyelitis in the 1920's and the abandonment of such treatment since, because of control studies carried out in 1931.[43, 44] I had a unique opportunity to observe in 1924 a series of forty-six early poliomyelitis cases, which revealed no statistically significant difference between treatment with convalescent serum and normal horse serum. Scant attention was paid to this report[45, 46] and I, myself, failed to press the point, but since then there has remained with me the lesson of the predominant need for controlled studies in highly variable disease entities.

Streptococcus infections of the pharynx or tonsils correspond to scarlet fever without a rash, and the results with sulfanilamide therapy appear to me equally unimpressive. Rhoads and Afremow[47] in a small but carefully controlled series of cases of sore throat could observe no beneficial effect from sulfanilamide on the severity or duration of the illness or on the incidence of complications, and they question the advisability of using the drug routinely in the average uncomplicated case of tonsillitis or pharyngitis due to hemolytic streptococci. It should be recalled, furthermore, that early experimental work has shown that sulfanilamide is likely to behave differently with organisms of low virulence.[17, 48] Many physicians, however, administer sulfonamide preparations for any sore throat without even considering a bacteriologic diagnosis. A number of highly placed clinicians condone this practice, and the routine use of sulfonamide preparations in scarlet fever and mild streptococcus diseases now appears to have official sanction.[49]

In the treatment of most cases of acute suppurative otitis media and mastoiditis of streptococcal origin, physicians generally feel that sulfanilamide is indicated. Long[26] advocates giving the drug routinely in the earache stage. Some have emphasized the masking effect when mastoiditis is threatening.[50] Horan and French[51] report that in a series of 621 cases of acute suppurative otitis media treated with sulfanilamide, the incidence of mastoidectomies was only 3.4 per cent as compared with 22.7 per cent before the introduction of the drug. I wish that a paper by Fowler,[52] entitled "Otitis Media and Its Extensions," could be made compulsory reading for all pediatricians. His tabulation (Table I) of factors that might have an influence in a case of otitis media should alone cause the drug enthusiasts to pause. He suggests that in simple otitis media one might delay chemotherapy until a week or ten days after the onset, when a sufficient dosage of a sulfonamide drug for three or four days should give the answer; drainage, when it has to be instituted, may be supplemented with chemotherapy for its effects on the "unreachable nooks and crannies of the temporal bone."

TABLE I

FACTORS IN OTITIS MEDIA*

1. Age	Infants and old people apparently more susceptible
2. Sex	No essential difference
3. Place	Flora and fauna vary in different vicinities
4. Environment	
5. Station in life	Clinic patients seem to have more trouble than private patients
6. Habits	Blowing of nose, swimming, etc.
7. Diet	Vitamins, etc.
8. Previous infection and immunity to infection	
9. Mode of infection	
10. Time	Yearly cycles of incidence; March and April peak, etc.
11. General physical condition	Debilitating disease
	Allergy
12. Heredity	Race
	Susceptibility to infection
	Anatomy
	Pneumatization of the temporal bone
	Type of Eustachian tube, diameter, curvature
	Lymphoid diathesis
13. Skill of physician and nursing	
14. Reaction to surgery	
15. Reaction to medication	Sensitivity
	Tolerance
	Vomiting
	Excretion, etc.
	Individual response
16. Type of infection	
17. Chance	

*Fowler, E. P., Jr.: Bull. New York Acad. Med. 16: 24, 1940.

Last year an English medical monthly[53] devoted its January issue to a symposium on the use and abuse of sulfonamides. Whitby and others write understandingly of the enthusiasm which has overrun critical judgment. While allowing considerable latitude when based on clinical

experience and judgment, they deplore the haphazard exhibition of these new drugs, the tendency to neglect routine clinical and laboratory examinations, and the prolonging of an adequate course of a particular sulfonamide drug beyond a period of five to seven days when no clinical effect has been observed during that time.

With respect to the use of the chemotherapeutic drugs in prophylaxis, an even more critical approach is needed. Information is lacking as to the incidence, in unselected population groups, of streptococcus disease and the proportion that may be expected to become seriously ill. It requires observation of large numbers of people over a considerable time before any reliable evidence can be forthcoming. I am not unmindful of the most recent report [54] of the use of sulfanilamide in the prophylaxis of rheumatic fever which has employed controls and statistical analysis, but even so the procedure cannot be considered finally evaluated yet.[55] It needs to be considered, furthermore, that in the use of sulfanilamide for the prophylaxis of rheumatic fever, as well as for the prophylaxis of infections in surgical conditions, there is the endeavor to prevent the occurrence of serious complications that are not uncommon.

SUMMARY

It might be re-emphasized that bacterial chemotherapy has revolutionized the prognosis and treatment of certain acute beta hemolytic streptococcus infections. There is already reason to believe that the advent of chemotherapy has ushered in a period of therapeutic advance even greater than that which marked the introduction of diphtheria antitoxin forty years before.

In general, patients will always have a better prospect of recovery if treated scientifically. In addition to having the requisite knowledge of clinical and laboratory aspects of disease processes, it is necessary to be fully conversant with the pharmacology of the individual chemotherapeutic substances. Because of the lifesaving results in certain severe streptococcic diseases or in serious complications of the less severe infections, the clinician is justified fully in starting chemotherapy on the basis of clinical diagnosis without waiting for the bacteriologic reports. On a pragmatic basis, one patient cured gives greater satisfaction than a number of fully investigated dead ones. Severe illness justifies the incurring of certain risks, and therefore the fear of toxic manifestations must not be allowed to interfere with the employment of full and effective dosage.

The new method, however, is still subject to many limitations, and we still do not possess perfect chemical agents that will destroy the bacteria while leaving the body cells completely unaffected. Therefore, in the treatment of a mild disease, or in attempts at prevention, there is hardly justification in incurring greater risks than are present in the condition itself. One does not use a duck gun on sparrows. It even may be conceded that with newer studies and developments in the field of chemotherapy, many of the present most sanguine hopes from therapy and prophylaxis may be realized, but we lay ourselves open to criticism if we depart from scientific method and critical approach. It would seem that at this time, members of a group like ours may well grasp whatever opportunity is afforded us to set up controlled clinical studies of sufficient size and scope to give the profession trustworthy indications.

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TENTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

MEMPHIS, TENN.—NOV. 18-20, 1940

Round Table Discussion on Neonatal Asphyxia

Chairman: Stewart H. Clifford, M.D., Boston, Mass.
Associates: Wyman C. C. Cole, M.D., Detroit, Mich.
Clement A. Smith, M.D., Boston, Mass.
Secretary: Maurice J. Lonsway, M.D., St. Louis, Mo.

CHAIRMAN CLIFFORD.—Some degree of asphyxia attends every normal birth. As the severity or duration of the anoxemia increases, however, physiologic and pathologic changes take place that may involve every organ and tissue in the body and result in a wide variety of clinical symptoms at or following birth. These changes may produce permanent damage, particularly in the nervous system.

This discussion will attempt to emphasize the fact that asphyxial changes involve the organism as a whole even though symptoms referable to one organ, such as the lungs or brain, may dominate the picture.

Asphyxia is far and away the most important cause of disease in the newborn period. It has been found to be the chief cause of death in 58 per cent of the infants autopsied at the Boston Lying-in Hospital since 1931.

The discussion will consider the problems of asphyxia at various fetal ages: first, in utero; second, during delivery and immediately post partum; and third, during the neonatal period.

The discussion for each age period will develop, in so far as is practical, along the following general outline:

I. Normal physiology
II. Cause of anoxia (anoxic, anemic, stagnant, or histotoxic)
III. Physiologic effects
IV. Pathologic effects
V. Clinical effects
VI. Treatment
VII. Prophylaxis

Asphyxia in Utero

Clement A. Smith, M.D., Boston

In the final analysis, respiration means the provision of oxygen to the tissues and the removal of carbon dioxide from them. A sufficient degree of interference with this process, whether in the tissues of the adult individual or in those of the fetus in utero, results in asphyxia. In the ordinary extrauterine individual this is accompanied by rather dramatic and widespread signs and symptoms. Unfortunately for our purposes, the manifestations of intrauterine asphyxia, though perhaps equally far-reaching and dramatic, are not nearly so evident to outward view.

In order to understand the respiratory relationship between the fetus and its environment and to discover at what critical level asphyxia might begin to jeopardize fetal existence, we must begin by describing the normal. I assume that our concern is with human physiology. Let us confess that we know decidedly little about the normal human fetus. Let us begin by stating that little bit and then add to it what can be inferred perhaps as applicable from the larger volume of animal studies.

The fetus is dependent on the maternal circulation to bring it oxygen and to remove its excess carbon dioxide. Therefore, it would seem impossible for the blood of the fetus to be any better oxygenated than that of the mother (if as well) or to contain any less carbon dioxide than is present in the maternal vessels (if as little). The only ways the fetal organism could avoid these limitations placed upon it by its situation would be by having hemoglobin peculiarly constituted so as to retain selectively more oxygen than the mother's blood could hold at any given tension, or, on the other hand, by having blood chemically able to give off carbon dioxide at tensions where the mother's blood could still take it up. While beneficial adjustment of the oxygen dissociation curve has been shown to occur in the fetal hemoglobin of certain animals,[1] there is no agreement as yet that the situation is so happily arranged in the human species. There is some evidence that the carbon dioxide dissociation of human blood at birth is such that the fetus can release this gas while the maternal blood is still able to take it up.[2] There are, however, no data whatever as to the carbon dioxide or oxygen dissociation curves during the more important months of fetal life before the infant is ready to be born.

Thus, in the light of present knowledge, all we know is an upper level above which the human fetus can hardly be expected to raise its oxygen supply. That is the level of oxygen in the maternal arterial blood (some 16 vol. per cent). We have a lower level below which the fetus cannot decrease its carbon dioxide; that is the carbon dioxide tension of maternal venous blood (about 42 mm.). Besides this "second-place" situation of the fetus, we know that it has a relatively inefficient circulatory system for purveying to its entire body the arterial blood it receives from the cord. Comparatively well-arterialized blood must reach the liver and may supply the brain, but the tissues of the lower half of the body and the abdominal organs in general are recipients of blood just as venous as that returning to the placenta to be reoxygenated.

Fortunately, we know a great deal about the oxygen and carbon dioxide levels as measured chemically in the blood supply immediately after the fetus has left the uterus.[3] But what we really want to know is the chemical situation of the human fetus in utero. Here, we have only two bits of information, and these are contradictory. Eastman[3a] found, on opening the human uterus before labor and quickly removing a loop of cord, that the umbilical vein blood (going from placenta toward fetus) contained about 13 c.c. of oxygen per 100 c.c. of blood, or, as it is expressed, 13 vol. per cent oxygen. The blood returning to the placenta in the umbilical arteries contained about 6 vol. per cent oxygen. On the other hand, the German investigators, Haselhorst and Stromberger,[3b] on averaging the results from eight specimens so secured, found figures of 3.5 and of less than 1 vol. per cent oxygen in these respective vessels. Both the American and the German authors agree very closely on other figures, such as the oxygen levels of cord blood at normal birth which are about 10 vol. per cent and about 3 vol. per cent. But Eastman's figures show the unborn fetus slightly better off for oxygen than it might be later at birth, while Haselhorst and Stromberger find its oxygen level much lower before labor than at birth. There is recent evidence to suggest that Eastman is nearer the truth of the actual situation, but it is only inferential. We know nothing at all as to the quantitative oxygen situation in the human fetus during all its preceding months of existence.

One thing seen in all human cord blood studies is the difference in oxygen levels of arterial blood reaching the fetus from those of venous blood leaving it for the placenta. This fetal arteriovenous difference is one of several volumes per cent. In other words, the oxygen left behind by the blood circulating through the fetus is a fairly respectable amount. But, by comparison with the adult situation, this oxygen is available only at a lower tension or head of pressure, and there is less of it in reserve. The fetus seems to operate on a somewhat smaller margin of safety than does the adult.

It is known that the infant at and soon after birth is supplied with erythrocytes and hemoglobin in an excess amount and to a degree suggesting comparison with the blood of an adult dweller at high altitudes. Although surprisingly few figures are available as to red cells and hemoglobin during fetal life in man, a rather complete recent series by Wintrobe and Schumacher[4] shows the excess of erythrocytes and hemoglobin to be a feature of late fetal life only. These workers found the blood of the average human fetus to have less than 4,000,000 red blood cells and proportionately low hemoglobin at seven months of gestation. It is interesting to note that recent workers[5] are discovering the blood of the infant at a few days of age to be actually higher in red cells and hemoglobin than was the blood from the cord at the moment of birth. Apparently this is not merely a matter of hemoconcentration. It suggests that the slight rise after birth is the last crest of a wave which began to pile up earlier in gestation and continued its increase even after parturition. This in turn suggests that the fetus may be pressed increasingly for oxygen during the last part of intrauterine existence; but these again are inferences.

To come back to matters of fact rather than speculation, clinical observation has shown that when the human fetus suffers a sufficient interruption or disturbance of the uterus-placenta-cord lifeline, the beating of its heart is altered, it may make tonic movements resulting in the expulsion of meconium, and it may make gasping movements of the respiratory apparatus. Sudden respiratory movements of this sort have been observed following circulatory interference in a human fetus as young as eleven weeks.[5] Such a response may be from either too little oxygen or too much carbon dioxide, or both. We know that toward the end of pregnancy many human fetuses apparently not disturbed by circulatory interference make rhythmic movements of the respiratory muscles in utero,[6] but we know that these movements, although sometimes continuing for an hour or so, are inconstant phenomena. What we do not know is whether they are a part of the fetal life of every human baby.

Perhaps this meager list of facts about the human fetus can be extended slightly by the inclusion of an important observation concerning the fetal lung. We know that whether or not it has undergone fetal exercise, the lung is a wet and soggy tissue which must at the moment of birth begin the process of conversion into a buoyant air-filled organ. This has been shown to be a process requiring more effort on the part of the thorax than will be needed later to maintain expansion.[7]

In summary, what knowledge is available suggests that in spite of low oxygen needs for heat and energy, the human organism during its fetal existence comes considerably nearer definite oxygen lack than during its ordinary existence thereafter. Under these circumstances it builds up an ever-increasing supply of hemoglobin and erythrocytes. Its respiratory center seems not to function sensitively, although it responds to sudden severe asphyxial circumstances with gasping, and at other times may motivate gentle, rhythmic, and prolonged respiratory muscle movements. In spite of these, expansion of the lung after birth requires an effort out of proportion to that needed for respiration later.

A great deal more than this has been learned by observation and experiment upon the fetuses of various animals. It must not detract in any way from this work to advise a certain amount of caution in applying such knowledge to the human

situation. One can urge this because a very striking thing about the work upon animals is that fetuses of various animal species have been shown to differ one from another. With this reservation, let us consider a few of the important observations upon experimental animals, and, in doing so, touch briefly on their implications for the human subject.

A first and general observation which has come from the work on animals is that the fetus is not the same sort of physiologic mechanism during its entire intrauterine existence. As the time for birth approaches, many fundamental things about the fetus are quite different from what they were halfway through gestation. For instance, while it is true that the fetuses of certain animals, notably the sheep, goat, and cow, have been shown to possess hemoglobin with a different oxygen dissociation curve from that of the mother, this difference is considerably more profound during certain regions of mid- and late gestation than it is as term approaches.[1a] In fact, maternal and fetal curves which are quite widely separated at eighteen or nineteen weeks of gestation in the goat have approached one another very closely by the time the kid is born at twenty-one weeks.

Another observation of somewhat the same purport is that which indicates that the oxygen saturation of blood is far from constant during the course of fetal life. Barcroft, Kennedy, and Mason,[8] who have studied this matter throughout the life of the sheep fetus, have shown that the oxygen levels in that organism display a fairly regular rise to the ninetieth or one-hundredth day of gestation, at which time the blood in the umbilical vein may reach an oxygen saturation of 90 per cent or more. This is almost as high as that of the adult animal. From then until near delivery, which occurs on about the one hundred and fortieth day, there is a gradual falling off to 70 or 80 per cent saturation, with a final drop in the last days of fetal life to 60 or 70 per cent. This work was done with extreme care, for another thing which Barcroft and his colleagues have shown is that the more one manipulates the placenta, uterus, and umbilical cord, the lower will be the oxygen values obtained from cord samples. In fact, the recent work of these authors makes it seem as though the fetus in utero may not be nearly so poorly off for oxygen as earlier work had indicated. It must be remembered constantly that our chemical determinations on the human fetus and the human infant at birth have been made after considerable manipulation, which usually consisted in the rather stormy activities of childbirth itself.

Another observation is the tendency for hemoglobin and erythrocytes to increase in late fetal life in animal just as in the human being. This, along with the course of oxygen levels just recounted, would indicate the probability that the human fetus does face a gradually increasing physiologic anoxemia during its later intrauterine life. However, we must guard against accepting too easily the idea that in the major portion of pregnancy, the fetus is a constantly oxygen-starved organism.

Of late, there has been much very interesting work done upon fetal animals with regard to rhythmic movements of the respiratory muscles.[9] There seems to be no doubt that such movements do occur, but it also seems to be quite definite that they do not occur constantly nor in all fetuses in any litter. Attempts to prove their significance by causing the maternal animals to breathe various chemical mixtures which would alter the gas relationships in the maternal blood and thus in that of the fetus have resulted in extremely contradictory data. One thing occurs in the rabbit fetus,[9] another in the cat,[10] and still another in the sheep.[11] When one considers that the rabbit fetus is born at thirty-one days, the cat at seventy, and the sheep at one hundred and forty, this is not very surprising. We seem so far from having the last word upon this subject that caution is indicated in applying any of these observations to the human species.

In our present state of knowledge, one can hardly believe that the fetal respiratory center is not somewhat depressed, or at least less responsive than that of the extrauterine individual. It seems also almost inescapable that the fetus must live under states of oxygen deprivation and possible carbon dioxide excess which would disturb your respiratory apparatus and mine considerably and would possibly also disturb other parts of our bodies. Whether low oxygen or high carbon dioxide tension is better borne by the fetus is somewhat in doubt. There is a little evidence from the work of Eastman that the fetal respiratory center is not very sensitive to carbon dioxide excess and that it is somewhat more sensitive to oxygen lack.

Now, all this poorly defined state of partial anoxemia in which the fetus may find itself and which appears to increase as the time of birth draws near does not mean that too much further anoxemia can be well borne by it. Those violent muscular and gasping movements, which, as mentioned above, may be shown by the human fetus on interruption of the cord circulation, indicate that the fetus does not meet anoxemia below a certain level without signs of trouble. You will hear something, I hope, of the various types of anoxemia which are recognizable physiologically, or rather pathologically. Barcroft has classified them as anoxic, anemic, and stagnant. Recently, Peters and Van Slyke have added a fourth type, histotoxic. In general, anoxic anoxemia signifies a situation in which the tension of oxygen in the arterial blood is lower than normal, and the hemoglobin is unable to become saturated to its usual extent. This could be called the physiologic anoxemia of fetal life. If aggravated, it is the condition most likely to inflict serious anoxemia upon the fetus, for, in general, it should be remembered that anything which disturbs the efficiency of respiration or circulation of the mother, anything that alters the air she has to breathe, such as the addition of too much nitrous oxide gas to it, and anything that reduces the close apposition of the placenta to the uterine wall will lower the tension of oxygen in the arterial blood available to the fetus by means of the cord. It is rather doubtful that the anemic type of anoxemia occurs very often, except perhaps with such conditions as fetal hydrops, where the blood becomes a very poor oxygen carrier. Stagnant anoxia may occur in situations which result in pressure upon the cord or knotting of it. Histotoxic anoxemia undoubtedly occurs from any factor which lowers the functioning integrity of the cells of the respiratory center and the tissues of the body, but among such factors the leading place must be given to anoxic anoxemia. Thus, we find one type of anoxemia leading to another.

I must confess that we do not know all the ways in which the fetus may be affected. I think we can believe, however, that it is affected not just in the lungs or in the central nervous system, but very possibly through many of the tissues of the body. Another thing I should like to point out is that an asphyxial crisis in the life of a fetus may occur without anyone knowing about it. If the obstetrician is listening to the fetal heart at the moment, a considerable change in its beat may be perceived, and he may make a diagnosis of fetal distress. But there is so much time during pregnancy when no one is listening to the fetal heart that a number of infants must be born who have weathered unsuspected anoxemic perils, or have not weathered them.

A final conception which should be made quite clear and which has been hinted at above is that anoxemia in utero may produce a living infant, able to breathe, but with considerable inefficiency. This inefficiency is due to anoxemic damage to the respiratory center cells and very probably also to mechanical damage to the lungs from gasping aspiration of amniotic sac contents, or possibly from actual edema of the lung tissue. What is the result? Further extrauterine anoxemia when the infant is cut off from the maternal circulation by birth and must use his lungs and respiratory center to satisfy his oxygen needs. Deleterious effects in other

parts of the body have been described by Dr. Clifford; I hope he may discuss this point further. The effects bear out the familiar statement that "anoxemia not only stops the machine, but wrecks the machinery."

So gradually may intrauterine blend in with extrauterine asphyxia that I shall not attempt to formulate a separate outline of treatment for these babies. That should emerge from the discussion. I also think it would be tedious to consider prophylaxis of intrauterine asphyxia in detail, since so many physiologic and pathologic aspects of the maternal organism would require exploration. Trace in your imagination a molecule of oxygen from the fetal respiratory center back through the umbilical cord, the placenta, the uterine sinusoids, the maternal arteries and aorta, the maternal pulmonary circulation, the lungs, and the upper respiratory tract until you finally come to the external atmosphere from which it came. This is a long chain, or bucket brigade, every member of which must function properly if intrauterine asphyxia is to be avoided.

Certain accidents are particularly apt to occur. The premature separation of the placenta, for example, may cause partial or complete cessation of the function of this bucket brigade. But it is possible for the brigade to break down anywhere along its course or for it to be given in its buckets insufficient material (oxygen) with which to start.

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Asphyxia During Delivery and Immediately Post Partum

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Until the past five or six years no one has ever paid a great deal of attention to asphyxia of the newborn infant. If a baby was stillborn, it was merely regarded as one of those things over which we had no control. It if was asphyxiated but ultimately breathed, it simply was classified as asphyxia livida or asphyxia pallida and usually forgotten. Seldom was any correlation made between asphyxia at birth and abnormal conditions which might later appear in the individual.

However, in the last few years certain important additions to our knowledge of intrauterine respiration and of the changes produced in various tissues of the body when they are deprived of an adequate supply of oxygen, even for very short periods, have placed an entirely new significance upon the baby that does not breathe immediately after birth. Another phase of this subject which has added greatly to the interest in it and to active discussion with the obstetricians has been the tremendous increase in the use of obstetric analgesia which has occurred during this same period.

As has been pointed out by Dr. Smith, our conception of fetal respiration and the inauguration of extrauterine respiration has been changed completely. It was formerly thought that the normal infant was born in a state of physiologic apnea and that as the placental circulation ceased to function, the accumulation of carbon dioxide in the baby blood stimulated the respiratory center and caused respiration to begin.

It is now generally believed that the mechanism of respiration is established long before birth and that regular respiratory movements occur during the latter third of intrauterine life. According to one school of thought, there is essentially no difference between intrauterine and extrauterine respiration except that gaseous exchange takes place through the placenta instead of the lungs. If this conception is correct, extrauterine respiration should begin at the instant of birth, not as the inauguration of a new function, but as the continuation of an already established process.

For the past six months, we have been timing with a stop watch the interval which elapses between the birth of the head and the establishment of respiration in every baby born at our hospital. It can be said absolutely without question that the normal baby takes its initial gasp within two seconds and cries within five seconds, and that regular respiration is established within ten seconds after the head is born. Certainly a delay for as long as thirty seconds is definitely abnormal and in most instances can be traced to some known factor.

I recently had the opportunity of seeing a baby apparently cry in utero. A woman was being delivered by cesarean section under spinal anesthesia. Fortunately the baby's face was directly under the incision. Before the amnion was opened, we could clearly see the baby making movements exactly like crying, and when the first nick was made in the amnion and air allowed to enter, the baby cried instantly and continued to cry lustily until delivered. Obviously this baby merely continued to do what he had been doing before.

This places an entirely new significance upon the baby that is not breathing at birth. Some very profound influence is necessary to make an older individual stop breathing. It is quite logical that an equally profound influence should be necessary to make a newborn infant stop breathing, whether that influence be simple strangulation, intracranial injury, shock, necrosis, or anesthesia. Accordingly, we must regard any baby that does not breathe within half a minute as abnormal and in danger of asphyxia.

Perhaps even more significant than this changed conception of respiration has been the demonstration of the tissue changes produced, particularly in the brain, by even very short periods of insufficient oxygen. Dr. Smith has explained the various types of cerebral anoxia and the method of their production. It is important to emphasize that about four minutes is the maximum time that brain cells can survive without some oxygen, and that in many cases irreversible changes may occur in less than one minute.

We have long recognized "birth injury" as the cause of a variety of degenerative lesions of the nervous system, but we have usually thought of this in relation to hemorrhage or direct trauma. From what we have learned of the changes produced by anoxia, it seems evident that many, if not most of these conditions, are probably the result of anoxic changes associated with asphyxia at birth and are not due to direct injury.

Dr. Frederic Schreiber has collected a series of well over one thousand cases of children with spastic diplegia, cerebral atrophy, epilepsy, mental deficiency, and other nervous lesions in which the only apparent etiologic agent was severe asphyxia at birth.

Schreiber, Kimball, and Whitley have recently completed a study of a series of Detroit school children which is very interesting. Three series of children were selected by the school authorities without the investigators knowing their identity. These consisted of backward children in special rooms in school, siblings of these children, and normals. The hospital birth records of these children were then studied with reference to asphyxia at birth. The ratio of asphyxia in the siblings and normals was the same, but it was four times as great in the subnormal group. This ratio would undoubtedly be many times greater if the spastics were also included, but this study involved only children able to attend school. The relationship between asphyxia at birth and serious degenerative changes in the nervous system seems, in my opinion, to be definitely established.

In the past, asphyxia has been classified poorly in most textbooks. Sometimes it has been defined simply as asphyxia livida or asphyxia pallida. These terms describe only the degree of asphyxia and tell us nothing whatever about its etiology or treatment. Sometimes it is classified as asphyxia of intrauterine origin and asphyxia of extrauterine origin. Here again we learn nothing about etiology or treatment, and it certainly makes little difference to the baby, as far as the physiologic and pathologic effects are concerned, when the asphyxia occurs.

Strictly speaking, asphyxia is a reduction in the amount of available oxygen in the circulating blood. Asphyxia is the commonest cause of cerebral anoxia. In general, there are two ways in which asphyxia may be produced in the infant at the time of delivery. There is asphyxia of central origin, and there is asphyxia of peripheral origin.

By asphyxia of peripheral origin is meant asphyxia resulting from some interference with the entrance of oxygen into the circulation. This may occur in utero from such conditions as premature separation of the placenta, interference with the circulation of the umbilical cord, or asphyxia or anemia of the mother. Or it may occur after birth from simple strangulation from foreign material in the air passages, or from atelectasis. In general this type of asphyxia is due to some accident of labor or some other condition over which we have relatively little control. Fortunately it comprises only a small number of the total cases of asphyxia.

By asphyxia of central origin is meant asphyxia resulting from some interference with the function of the baby's respiratory center. This may be due to direct cerebral injury as occurs in hemorrhage, laceration, or edema; it may result from toxins in the blood; it may come from the circulatory changes associated with shock; and particularly it may be the result of narcotics and anesthetics administered to the mother during labor. Here again, the asphyxia may occur before, during, or after delivery. This type of asphyxia is by far the most common and fortunately the one over which we can exert the maximum amount of control.

In our observations, more than 25 per cent of all newborn infants show some interference with the normal establishment of respiration. About 2 per cent are stillborn, about 15 per cent require resuscitation, and about 10 per cent show delayed respiration but ultimately breathe spontaneously.

A great many factors contribute to the production of asphyxia, and in a great many cases several of them operate together. This adds greatly to the complexity of the picture and makes it difficult to decide which of the various factors is predominant.

First of all we have factors related to the mother. The incidence of asphyxia is more than twice as great in cases in which the mother is sick, particularly in toxemia. It is more than twice as frequent in primiparas and shows a direct increase in proportion to the mother's age. Disproportion between the baby and the mother's pelvis is a major factor.

Greatest of all single factors is prematurity and immaturity of the fetus itself. Stillbirths are fifteen times as frequent among premature infants, and severe

asphyxia is more than twice as common. It is worthy of note that the larger the child, the less frequent is the occurrence of asphyxia. This undoubtedly is due to the fact that the respiratory mechanism is better developed in the more mature ones and that they are proportionately less susceptible to the effects of trauma, anesthetics, and narcotics.

All factors which tend to increase trauma to the baby tend to increase asphyxia. The longer the labor, the higher the rate of asphyxia. In all operative obstetrics the occurrence of asphyxia is many times that in spontaneous birth. Here also we have the added factors of deep anesthesia usually employed in operative obstetrics. Trauma acts in two ways, either causing direct cerebral injury or causing shock.

The greatest interest has centered around the influence of sedatives and analgesics administered to the mother to relieve the pain of childbirth. In an analysis of 5,000 consecutive deliveries at the Woman's Hospital in Detroit, which we made a couple of years ago, it was shown that every additional dose of any sedative or analgesic increases the incidence of asphyxia in direct proportion to the amounts given. Some of these, such as the barbiturates and morphine, act through direct depression upon the respiratory center. Others, such as scopolamine and paraldehyde, which are not essentially respiratory depressants, act either by prolonging labor or by having a direct histotoxic effect upon the brain cells. In ordinary normal cases, reasonable doses of properly selected sedatives given under controlled conditions probably do relatively little harm, but where large doses are used to accomplish the abolition of all pain and particularly in long labors and complicated deliveries, they may be very harmful. In all cases of premature birth, the use of sedatives is definitely contraindicated.

Perhaps even more important than sedatives in producing asphyxia are the various anesthetics used in obstetrics. Strangely enough, the harmful effects of the sedatives were recognized early, although anesthetics have been used for a much longer time and their effect upon the baby has been given serious consideration only recently.

It is obvious that no general inhalation anesthetic can be given to a mother without also giving it to her baby as long as the placenta is still intact. All anesthetics either directly or indirectly depress respiration. All young children are highly sensitive to anesthetic agents and possess a very narrow margin of safety. Added to this is the normally low oxygen concentration in the fetal blood. It should be immediately evident that no considerable amount of anesthesia can be administered to the mother without directly affecting the respiration of the baby.

There is considerable difference in the manner in which various anesthetics affect the oxygen concentration of maternal blood, but probably of much greater importance is the variation obtained by different techniques used by anesthetists of indifferent skill and grades of carefulness. We were able to show that the longer an anesthetic was given, the higher the percentage of asphyxiated babies. The results in cesarean section were most illuminating. When general anesthesia was used, 3.5 per cent of the babies were stillborn, 23 per cent were severely asphyxiated, and only 58 per cent breathed immediately; but when spinal anesthesia (which, of course, does not affect the baby) was used, there were no stillbirths, only 4 per cent were severely asphyxiated, and 92 per cent breathed at once. In this series all factors were the same except the anesthesia. When general anesthesia was used, the babies were so deeply anesthetized in many cases that resuscitation was either difficult or impossible.

Probably the duration of the anesthetic is much less significant than the degree of anesthesia obtained. A woman conceivably might have a first stage anesthetic for an hour that would do her baby much less harm than would a third stage anesthetic for five minutes. We are currently making some observations on this subject in which

not only the duration of anesthesia is being studied but also the degree of anesthesia. While these data have not been analyzed yet, it is safe to say that very few babies whose mothers receive more than five minutes of stage III, plane I anesthesia, breathe in a normal manner, and I have yet to find a case in which plane II anesthesia was arrived at where respiration of the fetus began normally. This is probably one of the greatest contributing factors to the bad results observed in operative obstetrics. In a great many instances the asphyxia probably is due not so much to the operative procedure involved as to the deep anesthesia that it required to carry it out. Furthermore, I am not convinced that the anesthetic agent used is of material importance. What matters is the degree and duration of the anesthesia.

It should be pointed out that the worst results occur when a combination of these factors is present. Given a toxic primipara of advanced years, a long labor, some dystocia requiring operative procedure, repeated doses of sedatives, and topped off by a surgical anesthetic, the chances of getting a normal baby are practically nil. This is, of course, extreme, but there are a great many cases in which two or three of these factors are operative.

I should like to recommend urgently that whenever operative obstetrics is necessary, spinal or local anesthesia be used if possible, particularly in the case of premature birth.

Finally I would like to discuss briefly the methods used in the resuscitation of the newborn infant. While this is almost entirely up to the obstetrician, we can do much to change methods sometimes observed. Of course the ideal treatment of asphyxia is not to get it, but probably few conditions in medicine about which we have a reasonably sound physiologic knowledge are mistreated more commonly.

Such procedures as vigorous spanking, violent artificial respiration, the pouring of ether on the skin, forceful dilation of the sphincter, and hot and cold tubbing are little short of barbaric in the light of our present knowledge. Not only are they ineffective but in many cases may do great harm.

When we consider that the asphyxiated baby is frequently already in shock and frequently may have a cerebral injury, the additional shock involved in these procedures can do nothing but harm the infant. Moreover, it is very doubtful that any really seriously asphyxiated baby ever breathed in response to these methods. Any baby that responds to such treatment would have breathed anyway and breathes in spite of the treatment.

In general, there are three things to do in the resuscitation of a baby. First, and probably most important, keep the baby warm. One of the outstanding characteristics of shock is a drop in body temperature associated with circulatory collapse. Even in a warm delivery room the change in the external temperature to which the baby has been accustomed is about fifteen degrees. The asphyxiated baby must be covered immediately with a warm blanket, or in severe cases, immersed in a body temperature bath to maintain his temperature.

Second, remove foreign material from the air passages. The folly of attempting oxygen therapy or artificial respiration while the trachea or pharynx is blocked by mucus or blood should be apparent. This may be accomplished in several ways: by simple postural drainage with gentle milking of the trachea, by gentle swabbing of the retropharynx, or by aspiration. The best procedure is the introduction of a tube directly into the trachea which also may be used later for the administration of air or oxygen. This, however, requires considerable skill, but most hospital staffs are competent to do it.

Third, get oxygen into the baby's lungs. It is upon this subject that the greatest amount of discussion has taken place. There are several ways in which this may be accomplished, the commonest being by the application of a mask over the infant's face, by a tube in the trachea, or by mouth-to-mouth breathing. Innumerable so-called resuscitators are on the market which, in general, provide for oxygen under

pressure combined with various forms of artificial respiration. In my opinion, most of these are highly impractical and accomplish nothing that cannot be done without them.

They are complicated to operate and require a more or less trained crew, they easily get out of adjustment, and usually when wanted worst they are in some other room where it takes several minutes to locate them and get them into operation. When we remember that one or two minutes may be all the time there is at our disposal, it can be seen how futile is the time spent in running around looking for a piece of equipment which may not work after it is found. Heated discussion has taken place over the question of whether oxygen and carbon dioxide, straight oxygen, or plain air should be employed in resuscitation. Henderson and his followers, basing their opinion upon the stimulating effect of carbon dioxide on the respiratory center, feel that oxygen mixed with carbon dioxide should be used. However, Eastman and his group have shown quite conclusively that while carbon dioxide is a stimulant up to a certain point, beyond that the sensitivity of the center is reversed and carbon dioxide becomes a depressant. Moreover, in all severe cases there is already an excess of carbon dioxide present. From my clinical observation it seems that both of these schools of thought are correct. In mild cases of asphyxia, carbon dioxide and oxygen are better, and in severe cases, straight oxygen is indicated. Waters, from the University of Wisconsin, has called attention to the fact that straight oxygen should not be used in the treatment of atelectasis. If a lobe of lung is isolated and injected with oxygen, in a few seconds it is completely collapsed and atelectatic, due to the quick absorption of all of the oxygen. The presence of a neutral gas is necessary to maintain the expansion of the lung. Inasmuch as the lungs of all asphyxiated babies are atelectatic, it can be seen easily that expansion cannot be accomplished by pure oxygen, so that after all of the technical discussion there has been of this subject, we may find out finally that ordinary air may be the best mixture. From the point of view of ready availability and the chemical composition of the gaseous mixture, the old-time method of mouth-to-mouth breathing probably is not only as practical but also as scientific as any. The dangers in this method of course are the possibility of infection of the baby and the overenthusiasm of the operator who may readily exert enough pressure to rupture some of the alveoli.

Something also should be said about the various drugs which are employed widely as respiratory stimulants. While these drugs unquestionably produce a sudden stimulus to respiration, this action is almost immediately followed by a corresponding or even greater depression. Their use revolves around the question as to whether or not the value of the original stimulation more than offsets the following depression. Personally I cannot recall a case in which I could see that they were of the slightest value. My chief objection to them, as well as to the mechanical resuscitator, is that physicians frequently rely upon them to the neglect of the more fundamental procedures.

I am sure that if a baby is kept warm, if his air passages are open, and if available oxygen gets into the lungs, he will breathe, provided that the process has not gone too far or that some pathologic condition is not present.

Asphyxia in the Neonatal Period

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The effects of asphyxia involve the organism as a whole even though symptoms referable to one part of the body, such as pulmonary atelectasis or intracranial injury, may dominate the picture. The extensive pathologic changes and the variety of clinical symptoms found associated with asphyxia are explained best as the result of underlying physiologic changes brought about by anoxemia.

The basic physiologic effect of anoxemia is the production of an increased hydrogen-ion concentration in the body through an accumulation of carbonic and lactic acids. The hydrogen ion has a fundamentally different effect on nerve tissue than it has when it is acting on smooth and cardiac muscle. On nerve cells it induces the successive stages of stimulation, discharge of energy, and paralysis. On the smooth muscle of blood vessels and capillaries it produces loss of tone and dilatation, thus allowing the escape of plasma and hemorrhage. On cardiac muscle it produces loss of tone, dilatation, and eventually failure.

The pathologic changes that have been found following intrauterine asphyxia may be summarized as congestion, edema, hemorrhage, and tissue degeneration. The congestion of blood vessels was profound, involving every organ and tissue and extending to the finest capillaries. Edema fluid was observed in the subcutaneous tissue, in the muscles of the extremities and the heart, in the periadrenal, and peripancreatic, in the retroperitoneal tissue, in the capsule and stroma of the adrenals, the thymus, the liver, and the pancreas, in the pleura, the lungs, the subarachnoid space, and the brain, and in the peritoneal, the pleural, and the pericardial cavities. Petechial hemorrhages were found scattered extensively throughout the various organs, while greater degrees of hemorrhage were found in the lung alveoli and parenchyma, in the liver capsule and parenchyma, in the heart, the intestinal tract, the subarachnoid space, and the ventricles, and in the brain substance. Actual tissue degeneration was evidenced in the liver by varying degrees of fatty infiltration, marked necrosis, and dissolution of tissue accompanied by hemorrhage, and in the brain, by changes ranging from areas of ganglion cell degeneration to widespread encephalomalacia.

The clinical symptoms that have been observed in asphyxiated infants are the result of the physiologic and pathologic changes induced by anoxemia. The actual symptoms encountered and their severity depend upon the degree and duration of the anoxia and upon the susceptibility of individual tissues.

Symptoms referable to the nervous system are the result of the combined effects of asphyxia on the blood vessels of the brain and on the nerve cells themselves. The loss of tone and dilatation of the blood vessels of the brain with escape of fluid and even blood cause intense congestion of all vessels, perivascular and cerebral edema, petechial or larger hemorrhages in the brain substances, and a great increase in the amount of cerebrospinal fluid, which fluid may contain a variable amount of free blood. These changes may cause bulging of the anterior fontanel, separation of the sutures, abnormal increase in the size of the head, convulsion, interference with respiration, cyanosis and atelectasis of central origin, and gross neurologic damage. The successive stages of nerve cell stimulation, discharge of energy, and paralysis affect the brain centers, causing acceleration of the fetal heart, aspiration in utero, difficulty in resuscitation at birth, irregularities in respiratory rate and rhythm, cyanosis or atelectasis of central origin, muscular hyper- or hypotonia, convulsions, and permanent neurologic damage. The peripheral nerve centers likewise may be affected, causing extrasystoles (irregularities and slowing of the heart rate) and heart block.

The phenomena of asphyxia may be confined to the intrauterine period and recovery set in at birth, providing the lungs are capable of supplying adequate oxygen to the tissues. It is more common, however, to have the function of the lungs so interfered with by the fetal anoxia that they are unable to sustain a positive oxygen balance. Under these conditions the oxygen lack present in utero persists and may become more marked in extrauterine life, with the patient's clinical state becoming progressively more serious unless relief can be afforded. It is possible to have a relatively slight fetal asphyxia produce dangerous extrauterine anoxemia if, by chance, the fetal process seriously involves the lungs or the respiratory center.

Wilson and Farber have pointed out that the cohesion of the moist surfaces of the air passages in collapsed and airless lungs offers a considerable mechanical resistance to the entrance of air and that a relatively great force is required to overcome this cohesion during the initial expansion of an atelectatic lung. When this normal resistance to expansion was coupled with (1) an injured respiratory center, (2) an imperfectly developed thoracic mechanism, or (3) bronchial obstruction due to aspiration of amniotic sac contents, mucus, or blood, the state of atelectasis would be prolonged to a pathologic extent.

The above explanation does not seem entirely adequate to explain the type of atelectasis here reported. In our cases, while the factor of injury to the respiratory center was undoubtedly present to some degree, it was not sufficiently prominent to explain all the findings. Bronchial obstruction was decidedly not a factor. Another possible explanation suggests itself that is in keeping with the pathologic findings observed in other organs. In the presence of asphyxia the blood vessels of the lung undergo loss of tone and dilatation, allowing escape of plasma and red blood cells into the surrounding lung tissue and into alveoli. This process would explain the observed findings of congestion, edema, and hemorrhage in the lung stroma and in the alveoli. Thus an additional factor preventing the normal expansion of the lung may be present under certain conditions; namely, the increased turgor or resistance of the lung substance. While this hypothesis should be investigated further, it is in keeping with DeLee's statement, "We long ago gave up the notion that it is possible to inflate the atelectatic alveoli of the lungs. In 1902 I proved that air under 3 pounds pressure would not do it." Dr. Clement A. Smith of this clinic found that a much greater pressure was required to expand forcibly the lungs of an asphyxiated baby of the type here discussed than was required for ordinary infant lungs.* Our present clinical treatment of asphyxia is based on this hypothesis, and its success adds weight to the truth of the premise. We make no effort to expand the asphyxiated infant's lungs forcibly but keep him at complete rest in an atmosphere of 50 to 60 per cent oxygen. If the infant is to survive his general condition quickly improves in oxygen, and usually by the fourth day the x-ray and physical examination demonstrate expansion of the atelectatic areas. The point is of such great practical importance that more extensive studies are indicated.

There are numerous other clinical findings observed in asphyxiated infants that find their explanation on a physiologic basis. The liberation of edema fluid explains the findings of subcutaneous edema, sclerema, and fluid in the body cavities. The association of petechial hemorrhages with asphyxia is well known, but the importance of asphyxial bleeding in other locations should be stressed. Many of the gastrointestinal, pulmonary, and liver hemorrhages may be of this origin. Asphyxia, in the complete absence of trauma, may be responsible for varying degrees of hemorrhages into the cerebrospinal fluid, into the ventricles, and into the brain substance itself.

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*Dr. Smith's report on Baby G's lungs: The lungs show massive atelectasis following intrauterine asphyxia. "The lung is suspended in a jar and it responds to the rhythmic application of negative pressure as follows (measurements in cm. of water):

1. Minus 8 cm. for 5 min. No effect.

2. Minus 13 cm. for 5 min. Very little effect; about 1 c.c. of air in and out of lung with each 'breath.'

3. Minus 19 cm. for 6 min. First visible expansion of scattered areas of lung surfaces begins; coincidentally, definite emphysematous blebs appear.

4. Minus 22 cm. for 8 min. Further expansion, but still not including as much as 50 per cent of the lung surface; only 3 c.c. of air per 'breath.'

5. Minus 30 cm. for 2 min. Lung expands, but not completely and the blebs are larger; each 'breath' is about 8 c.c.

"By contrast, Baby A-40-26, a stillborn infant delivered the same day as Baby G, showed complete expansion at minus 22 cm. of water, and ventilation of about 10 c.c. per 'breath.' The cause of death in this infant was uncertain, but these figures are fairly typical of the 'normal' stillborn lung."

DISCUSSION

DR. WILLIAM F. WINDLE, CHICAGO.—I am sure that I cannot add very greatly to this beautiful exposition of the subject of neonatal anoxemia. There are a few concepts which might be given further consideration. I believe we should think of the oxygenation of the blood not as an unchanging phenomenon, but as one that varies from time to time. This is best observed in the latter part of gestation. Uterine contractions seem to regulate the amount and quality of blood going to the fetus in the umbilical vein. With each uterine contraction we can observe reddening of this stream of blood. With each relaxation period the blood in the umbilical vein turns bluish, and analyses show that it has less oxygen in it than just after contraction. Correlated with these changes in the oxygen content of the umbilical vein blood, we observe that the fetus becomes active when the blood is blue and quiets down when the blood becomes red. Similar behavior can be observed in the intact specimen. In the periods of activity the fetus sometimes executes respiratory movements, and it may aspirate amniotic content if the anoxemia becomes profound.

One may question whether the nerve cells of the fetus are as susceptible to asphyxia as are those of the adult. Recent work from the University of Minnesota by Kabat indicates that the nerve cells of the young animal resist asphyxia longer. I think this fact may offer a ray of hope; for if the fetal nerve cells were as susceptible as those in the adult, we would encounter far more instances of serious cerebral damage in the newborn infant which has experienced anoxemia during birth. One wonders what neurologic damage occurs in fetuses subjected to varied degrees of asphyxia. At this Round Table it has been shown that severe states of asphyxia may lead to marked disturbances of behavior after birth. I can add some confirmatory evidence from animal experimentation. We have seen neurologic symptoms develop after prolonged asphyxia at birth in the kitten. I recall one specimen in particular. This was the first born of a large litter of kittens; it was apparently dead at birth and was thrown aside as useless. Some twenty minutes later it was observed to gasp, although the amnion was still on it and it could not have breathed any air. Heroic efforts were then used to resuscitate this kitten. We were successful in keeping it alive for one month. It was spastic, showed marked tremors, did not gain ability to right itself for several days, and never cried, although it made efforts in that direction. Physically this kitten resembled certain human infants after birth injuries.

In asphyxia, the fetus commonly aspirates amniotic fluid. There is some recent evidence that when this occurs, the ductus arteriosus may close, at least temporarily. It seems probable that other changes of this sort, such as activation of the muscle of the gut, occur in the milder forms of asphyxia while the fetus is still in utero.

We have had some experience in resuscitation of fetal and newborn animals and have been interested in the question of the efficacy of carbon dioxide in oxygen mixtures for this purpose after the use of nembutal anesthesia during the delivery. I think we can say that the carbon dioxide is definitely contraindicated. The threshold of the respiratory center of the newborn kitten is raised by this drug to a level that cannot be reached by the concentration of carbon dioxide already existing during asphyxia. Consequently, when carbon dioxide is added to the alveolar air breathed by this newborn kitten, an insult is added to an already marked injury. The newborn kitten does not do as well under this treatment as under the treatment with oxygen-air mixtures alone. In fact it often dies. This is in accord with the recent views of Henderson on this subject, as published in the *Journal of the American Medical Association* in February, 1940.

I want to express my appreciation for being permitted to say these few words. I have enjoyed this round table greatly. The chairman of the round table, and the speakers are to be congratulated.

DR. LONSWAY.—Have you done any work on the effect of mothers' smoking cigarettes?

DR. SMITH.—No work has been done by us, although I believe Dr. Sontag of Yellow Springs, Ohio, has investigated this factor. His results suggested that the fetus might respond to the mother's smoking, but I think here we must remember how commonly in everyday practice one sees normal infants born to women who have smoked during pregnancy.

DR. H. F. GARRISON, JACKSON, MISS.—Would it be practical or feasible to use an electric stethoscope over the abdomen for a continuous observation of the fetal heart during labor?

DR. SMITH.—Such an instrument might be used, although many of the accidents we have discussed might occur before labor begins.

DR. E. L. TIMMONS, COLORADO SPRINGS.—Is there any way these symptoms of conditions that happen to the fetus prior to labor can be presented to the mother so she may protect herself? Is it important to keep the mother's hemoglobin content up during the latter part of the pregnancy?

DR. SMITH.—Most of what has been said applies, unfortunately, to unpredictable situations, such as placental separation, knotting of the cord, and so on. As to preserving the maternal hemoglobin at a high level, this would seem to be more valuable for the mother than for her baby. The baby suffers because of maternal anemia, unless it be so profound as to produce secondary fetal anemia.

DR. J. W. BRUCE, LOUISVILLE.—Would you prefer the baby's head to be elevated, lowered, or at the same level as the body? Would that also apply in cases of cerebral hemorrhage?

DR. COLE.—During resuscitation the baby should be placed face down with the hips slightly elevated to gain the advantage of gravity in clearing the air passages of foreign material. The practice of holding babies head down by the feet should be condemned, particularly if there is any likelihood of a head injury. After the baby has been resuscitated, the head should be elevated if a brain hemorrhage is suspected.

DR. ELDRIDGE, NEW ORLEANS.—Have any studies been made with other anesthetics besides ether?

DR. COLE.—Observations have been made on most of the common anesthetics. As we emphasized before, any general anesthetic is given to the baby as well as the mother. Probably more important than the type of anesthesia used is the duration and degree of anesthesia. The skill of the anesthetist in providing satisfactory anesthesia and at the same time keeping the patient adequately oxygenated is no small factor.

Our studies have shown that the incidence of asphyxia is in direct proportion to the duration of labor. Undoubtedly, trauma with its resulting shock is one of the most important predisposing factors to asphyxia.

DR. J. K. MACK, LOUISVILLE.—Would dilating the rectal sphincter do any good?

DR. COLE.—Any baby who is sufficiently conscious to respond to dilatation of the sphincter will respond just as quickly and much better if the methods previously recommended are employed without the danger of added trauma involved.

DR. H. KENNEDY, JR., BIRMINGHAM.—What effect does air conditioning in delivery rooms have on the newborn baby?

DR. COLE.—If by air conditioning is meant proper humidification, it certainly can be only of help. If air cooling is also implied, great care should be taken that the temperature of the delivery room is not below 85°, as the cooling to the exposed infant might contribute considerably to shock.

DR. G. J. LEVY, MEMPHIS.—How often in practice have ruptured air cells occurred?

DR. SMITH.—I should like to report some experimental work now in progress. We have subjected the lungs of all stillborn and newborn infants coming to autopsy during the last several months to tests for their mechanical efficiency. The lung is suspended in a glass jar, which serves as an artificial thorax and in which measured negative pressures are produced. The setup is the same as that devised by Wilson and Farber. We find that blebs due to rupture of alveoli may appear at from 25 to 35 cm. (water) negative pressure. Now, the infant himself has to apply a certain amount of negative pressure with each breath, and may apply quite a lot when he gasps suddenly. We have devised a method which measures the negative pressure applied by the living infant to his lungs and have been surprised to find 3-pound premature infants using forces of 30 and 35 cm. of water. In other words, nature herself seems to apply forces which we are wary of using with our machines.

DR. M. H. ROBERTS, ATLANTA.—Have you any figures on paraldehyde?

DR. COLE.—In a limited series of about 150 cases, less than one-half of the babies of mothers who received paraldehyde breathed immediately upon delivery.

DR. G. L. HACKER, DALLAS.—How many of the babies developing asphyxia do so because of central nervous system injuries?

DR. COLE.—That is an impossible question to answer, but if by central nervous system injury is meant all of the transient injuries, which include the effects of drugs and anesthetics as well as shock, I would think that at least 75 per cent are of this type.

DR. G. W. KUTSCHER, JR., ASHEVILLE, N. C.—What about mucous obstruction?

DR. COLE.—This may be a common cause of mild asphyxia and atelectasis but is usually apparent and responds readily to treatment. Persistent formation of excess mucus is, as Dr. Clifford has pointed out, usually an indication of more marked asphyxia with actual changes in the bronchi.

DR. W. M. TAYLOR, OKLAHOMA CITY.—Would you comment on the use of carbon dioxide and oxygen in getting the baby to breathe?

DR. COLE.—That is a difficult question, concerning which there are two widely divergent schools of thought. In general, when there is profound asphyxia, straight oxygen is the best; when the asphyxia is milder, carbon dioxide in addition seems to exert a more stimulating effect.

DR. D. J. BARNES, DETROIT.—Dr. Cole referred to the baby asphyxiated as going home as a well baby.

DR. COLE.—Correction. Apparently well baby.

DR. BARNES.—Do these babies go home well? Do these babies subsequently show damage or do they subsequently recover?

DR. COLE.—While no follow-up studies have been made upon enough of these cases to be conclusive, I am convinced, and I think most of you are, that this is an important factor in the development of subsequent degenerative disease of the nervous system as well as emotional and psychic instability.

ANNUAL MEETING, REGION I OF THE AMERICAN ACADEMY OF PEDIATRICS

New Haven, Conn., March 27-29, 1941

The annual meeting of Region I of the American Academy of Pediatrics took place March 27-29, 1941, at New Haven, Conn. The official registration headquarters were maintained at the Taft Hotel and the scientific sessions were held at the auditorium of the Yale Law School. The various states comprising Region I were well represented, a total registration of 223 Fellows of the Academy being recorded. In addition to the Fellows present, there was approximately an equal number of guests, making the total attendance something over 500.

The opening session, on the evening of March 27, at which Dr. Oliver L. Stringfield of Stamford presided, was devoted to a discussion of the influence of pediatrics in the present defense program. Dr. Martha M. Eliot, Assistant Chief, United States Children's Bureau, who had recently returned from England, read an interesting paper on the various problems involved in the care of the children evacuated from the large English urban centers at the outbreak of the present war. Dr. Frederick F. Tisdall, assistant professor of pediatrics at the University of Toronto, discussed the many contributions made by pediatricians in Canada, especially those involving the maintenance of adequate nutrition.

There were three scientific sessions at which a total of eighteen papers were read. At the morning session, March 28, with Dr. Joseph I. Linde of New Haven presiding, the clinical, diagnostic, and therapeutic problems related to streptococcal disease in children were discussed by Dr. Grover F. Powers and Dr. Paul L. Boisvert of New Haven; and by Dr. A. Clement Silverman of Syracuse, respectively. The problem of rheumatic fever, its incidence, its relationship to streptococcal upper respiratory infections, and its epidemiologic considerations were discussed in papers by Dr. O. F. Hedley of the United States Public Health Service; Dr. Ann G. Kuttner of Irvington-on-Hudson; and Dr. John R. Paul of New Haven, respectively. At the afternoon session Dr. J. Harold Root of Waterbury presided. The meeting was devoted to considerations of some orthopedic problems of interest to the pediatrician. The papers were presented by Dr. James D. Trask, Dr. Muriel Case Downer and Dr. Alexander L. Bassin of New Haven; Dr. Vernon W. Lippard and Dr. M. Beckett Howorth of New York City; and Dr. Winthrop M. Phelps of Baltimore. The subjects discussed included; various studies in poliomyelitis; the use of physical therapy; the treatment of congenital deformities; the community care of the crippled child; the cerebral palsies; and coxa plana. The meeting on March 29 was devoted to the problems of puberty and adolescence. Dr. Howard W. Brayton of Hartford presided. Papers were read by Lawrence K. Frank, vice-president of the Josiah Macy, Jr., Foundation; William W. Greulich, Director of the Brush Foundation, Western Reserve University; and Dr. Hilde Bruch and Dr. Ephraim Shorr of New York; Dr. Arthur H. Morse of New Haven; and Dr. Douglas A. Thom of Boston. The subjects discussed included growth and development of adolescent children, the relation of obesity to puberty, gynecologic and psychiatric problems of adolescence, and endocrine therapy.

On Friday, March 28, Dr. Richard H. Shryock, professor of American history at the University of Pennsylvania, delivered the annual Beaumont Lecture under the auspices of the Beaumont Medical Club of Connecticut, on the subject "The Advent of Modern Medicine in America." The lecture was well attended and enthusiastically received.

The annual dinner was held Friday evening, March 28, at the Grand Ballroom of the Taft Hotel, with Dr. Ernest Caulfield of Hartford as toastmaster. The

Academy was fortunate in having as its main speaker Odell Shepard, Goodwin Professor of English at Trinity College and lieutenant governor of the state of Connecticut. Mr. Shepard's address "The Unicorn's Horn as Materia Medica" was a most entertaining experience.

Two trips were planned for the members of the Academy and their guests on the afternoon of March 29. Dr. Arnold Gesell's Clinic of Child Development, at the Institute of Human Relations, Yale University, was visited by a large group who also saw an interesting cinema demonstration of the various clinical methods employed for infant testing and of various case studies. Another group were entertained at the Southbury Training School and Hospital, a new institution recently completed for the care and training of the mental defectives in Connecticut.

HERMAN YANNET, M.D.

Abstracts of Papers Read at Meeting of Region I

Streptococcal Infections in Children; General Considerations

Grover F. Powers, M.D.

From consideration of the patients who come to a university children's clinic unrestricted as to type of disease acceptable, one gets the impression that the majority of them fit into one or the other of two quite dissimilar categories: disorders of behavior, and acute infectious diseases. Of the latter there are two main groups; namely, the pneumococcus pneumonias and the diseases caused by the beta hemolytic streptococcus.

In regard to streptococcal infections, 4,800 records of admissions to the public children's ward service of the New Haven Hospital were studied. There were some 2,000 cases in Group I constituting admissions in 1934, 1935, and 1936, the years preceding the use of sulfanilamide, and some 2,800 cases in Group II constituting admissions in 1938, 1939, and 1940.

The results of the study show that the hemolytic streptococcus was found in the nose, throat, or pus in one of every seven patients admitted, and these patients had definite disease due to that organism; there were almost as many more children who harbored the streptococcus but who did not have a disease caused by that germ.

Scarlet fever and erysipelas are the diseases usually thought of as caused by the hemolytic streptococcus, but a more important form of infection is that found most commonly in children under 3 years of age called "streptococcal fever." These patients are ill for at least four to six weeks and are "not themselves" for a much longer period. They have moderate fever, mild sore throat, swollen glands of the neck, infected ears, and anemia. They have no appetite, and their dispositions are bad. Such children are altogether miserable.

Children who die from infections with hemolytic streptococcus usually have the germ in the blood. They often have erysipelas, meningitis, peritonitis, pus in the chest or mastoid cells, or the complications of scarlet fever. Sulfanilamide has reduced the death rate in these conditions from about 10 per cent in Group I to a little over 1 per cent in Group II.

The problem brought about by the hemolytic streptococcus in New Haven might be quite different in communities of different size or climate, and in house practice. In New Haven the disease is more common in the winter, spring, and fall months, but it is present in every month. It is important to follow the streptococcal infections in a family or school and also to find out, if possible, the influence of the streptococcus in patients who have the organism in the nose or throat but do not have a sickness primarily caused by streptococcus.

Diagnostic Procedures in Streptococcal Infections

Paul L. Boisvert, M.D.

There are certain clinical signs, in addition to a scarlatinal rash and erysipelas, which for all practical purposes are indicative of disease caused by the hemolytic streptococcus. These include: (1) the syndrome "streptococcal fever," described by Dr. Powers, which is seen in infants and young children; (2) the fiery red throat, often with tonsillar exudate, of older children; (3) swollen neck glands; and (4) discharging ear. With patients exhibiting a less obvious form of the disease, the presence or recent occurrence of any of these manifestations in other members of the family is often helpful in diagnosis.

In addition to bedside and familial epidemiologic methods, laboratory aids are available. Throat cultures are positive for hemolytic streptococci in a large percentage of patients with streptococcal disease, and in pediatric practice the presence of these organisms in the throat is significant. Nose cultures, although not as frequently positive as throat cultures, are highly specific and are of definite value in complimenting cultures of the throat. The recovery of hemolytic streptococci from any purulent lesion (skin abscess, blood, spinal fluid, ear pus, etc.) makes clear the diagnosis. In addition to cultural methods, there is a simple serologic test, the fibrinolysin test, for determining the presence of streptococcal disease.

Treatment of Hemolytic Streptococcal Infections

A. Clement Silverman, M.D.

It is hardly necessary to emphasize that sulfanilamide has revolutionized the prognosis and treatment of certain acute hemolytic streptococcus infections. There is reason to believe that the advent of chemotherapy has ushered in a period of therapeutic advance even greater than that which marked the introduction of diphtherin antitoxin forty years before.

After reviewing the pharmacology of sulfanilamide, the various aspects of its use in treatment are taken up. In connection with possible toxic reactions, particularly the most serious ones, attention is called to certain animal experiments from different laboratories which suggest the principle that a high protein, low fat diet may prevent damage to the liver and blood-forming organs. Because of the life-saving results in certain severe streptococcic diseases, the physician is justified in incurring certain risks, and the fear of toxic manifestations must not be allowed to interfere with the employment of a powerful remedy in full and effective doses. In serious streptococcal disease or complication, it is justifiable to start chemotherapy on the basis of clinical diagnosis alone, without waiting for the bacteriologic reports, for, on a pragmatic basis, one patient cured gives greater satisfaction than a number of fully investigated dead ones.

It is requisite, however, to be fully conversant with the pharmacology of the individual chemotherapeutic substances, in addition to having the necessary knowledge of the clinical and laboratory aspects of the disease process. The new method, however, is still subject to many limitations and the new chemicals are not perfect remedies that will destroy the bacteria while leaving the body cells untouched. The physician must therefore make use also of the older methods, including serum and symptomatic treatment, whenever necessary. In general, patients will always have a better prospect of recovery if treated scientifically.

The enthusiasm for new things, however, should not overrun critical judgment. In a mild disease, or in attempts at prevention, one is hardly justified in incurring greater risks than are present in the condition itself. One does not use a duck gun on sparrows. It would seem that a group like the Academy of Pediatrics should at this time accept the challenge and grasp the opportunity to set up controlled clinical studies of sufficient size and scope to give the profession trustworthy indications of when to use the newer chemicals and when to leave them alone.

Incidence of Rheumatic Fever

O. F. Hedley, M.D.

The importance of rheumatic fever as a public health problem, although long recognized by members of the American Academy of Pediatrics as a major catastrophic disease of childhood, is only beginning to be appreciated by the great mass of practicing physicians, the lay public, and even responsible public health officials. Thanks to the efforts of the Children's Bureau, a definite program has been inaugurated to combat this menace to the childhood of this nation.

Statistics regarding the incidence of rheumatic fever and rheumatic heart disease are still extremely inadequate because of failure to recognize the disease, poor terminology, and inadequate recording of deaths due to these causes. The establishment of state registers should render invaluable service by focusing attention on this problem in a definite geographic and administrative area; registers are not likely to prove successful unless supported by adequate treatment facilities.

Studies in Philadelphia indicated that in 1936 there were more deaths from rheumatic heart disease among persons under 20 years of age than from whooping cough, measles, meningococcus meningitis, diphtheria, scarlet fever, and poliomyelitis combined. Paul has shown that in New Haven this disease results in more medical admissions than other acute infectious diseases such as poliomyelitis, scarlet fever, measles, pertussis, and diphtheria, but fewer than the two major chronic infectious diseases, tuberculosis and syphilis.

In the United States as a whole there has been a substantial decline in deaths from heart disease among persons 5 to 24 years of age over a fifteen-year period, 1922-1936. This decline was greatest in the parts of the country which paid the most attention to rheumatic fever. These studies show that deaths from heart disease (mostly rheumatic heart disease) in this age period are greater in cities than in the country, in the north than in the south, and among colored persons. Although the geographic distribution indicated the highest mortality in the northern part of the country, it should not be regarded as a rarity even in the deep south. The highest mortality occurred consistently in Utah, a state with high altitude, low rainfall, and not excessively cold.

In Philadelphia during the five-year period, 1930-1934, there were 5,921 hospital admissions involving rheumatic heart disease, rheumatic fever, Sydenham's chorea, and subacute bacterial endocarditis. These diseases were present in 0.70 per cent of admissions from all causes; in three children's hospitals they were present in 1.56 per cent of all admissions. These conditions were indicated in 2.4 per cent of medical admissions to general and 5.8 per cent of medical admissions to children's hospitals. Over 93 per cent were ward patients. It is estimated that these conditions cost over $272,000 a year for hospitalization, exclusive of physicians' services, most of which are rendered gratuitously.

Despite the fact that the study embraced admissions to general as well as children's hospitals, it was found that the peak incidence of onset of rheumatic fever occurred in the 5- to 9-year age period, the mode occurring at 8.7 years. Over two-thirds of the cases of rheumatic fever had their onset among persons under 20 years of age; chorea was confined almost exclusively to the prepuberty age period. Rheumatic fever was somewhat less common among negroes, and chorea considerably less frequent. Rheumatic fever was almost evenly divided according to sex; rheumatic heart disease occurred slightly more frequently among females. Chorea was nearly twice as common among females. The clinical records of 63 per cent of the cases of rheumatic fever indicated diagnoses of heart disease. The percentage of cases of rheumatic fever with heart disease was greatest among persons under 20 years of age.

During this five-year period there were 916 deaths from rheumatic heart disease among these admissions to Philadelphia hospitals. The mean age at death was slightly under 30 years. The greatest number occurred in the 20- to 29-year age period. Nearly 75 per cent occurred among persons under 40 years of age. At least 3.5 to 4.5 per cent of first attacks of rheumatic fever terminated fatally.

The greatest number of admissions for rheumatic fever occurred during the spring months and were maximal in April. Considerable variations were noted from year to year. There was apparently no relationship between the amount of rainfall and the number of admissions from rheumatic fever and chorea. The seasonal distribution of deaths from rheumatic heart disease is not dissimilar from that of admissions; it is considerably different from the seasonal distribution of deaths from acute coronary occlusion.

The distribution of these cases of rheumatic fever, rheumatic heart disease, and chorea does not suggest that proximity to a water course is an important factor.

Observations on the Effect of Streptococcal Upper Respiratory Infections on Rheumatic Children

Ann G. Kuttner, M.D.

Three outbreaks of streptococcal upper respiratory infections occurring during three successive winters in a sanatorium for rheumatic children are reported. Each epidemic was associated with Group A beta hemolytic streptococci of a single type, but a different type was prevalent in each outbreak. The incidence of rheumatic recurrences following these three waves of streptococcal pharyngitis varied greatly. In the first outbreak, following a latent period, half the children showed signs of rheumatic activity; in the second, all the children escaped rheumatic sequelae; and in the third, a relatively small proportion developed rheumatic recurrences. A comparison of the two types of streptococci associated with recurrences (i.e., "effective" strains and the "noneffective" strain) failed to show any significant differences.

At the present time, there is, in our opinion, no adequate explanation of why rheumatic manifestations sometimes follow in the wake of streptococcal upper respiratory infections and sometimes do not. It seems possible that either the "noneffective" strains of Group A beta hemolytic streptococci lack some unknown, hypothetical factor necessary for the precipitation of rheumatic recurrences, or that the vulnerability of rheumatic subjects to the effect of streptococcal upper respiratory infections varies greatly from year to year.

Following infection with the two "effective" strains of streptococci, rheumatic recurrences developed sporadically over a period of months. It must be assumed, therefore, that these organisms carried the hypothetical rheumatic factor throughout the epidemics. However, a large number of children who had streptococcal pharyngitis due to these strains failed to develop demonstrable signs of rheumatic activity, suggesting that these individuals may have been in a refractory state. A comparison of the rheumatic histories of the children who did and those who did not develop rheumatic recurrences showed no striking differences.

An analysis of the previous rheumatic attacks of the fourteen children who developed rheumatic recurrences following streptococcal upper respiratory infections showed that the rheumatic manifestations in each patient tended to follow a certain pattern characteristic for the particular individual. Mild and severe rheumatic manifestations followed infection with the same strain of Group A beta hemolytic streptococci.

The effect of streptococcal upper respiratory infections in precipitating rheumatic sequelae has usually been studied in rheumatic patients with marked cardiac damage, who are known to be subject to frequent rheumatic recurrences. In this

study, children in the early stages of rheumatic fever were selected, because it is of primary importance to determine what factors precipitate recurrences before marked cardiac damage has developed. It has been found that in the majority of cases severe cardiac involvement occurs within five years after the initial attack of polyarthritis or carditis. At the present time, there is no way of predicting the subsequent course of a child shortly after his first attack of polyarthritis or carditis unless the first attack of carditis results in severe cardiac lesions. It is of interest, therefore, that thirty-one children who contracted the "effective" streptococcus Type XXVII pharyngitis within five years following their first attack of polyarthritis or carditis escaped rheumatic sequelae.

As far as explaining the role of Group A beta hemolytic streptococci in the etiology of rheumatic fever is concerned, our observations leave many questions unanswered. Although the total number of rheumatic recurrences, namely, fourteen, observed during the three winters among more than 300 rheumatic children is small, it is striking that all of these followed in the wake of streptococcal pharyngitis. No child who escaped streptococcal upper respiratory infections developed rheumatic manifestations. On the other hand, many children who contracted infections with the "effective" strains of streptococci remained well.

Rheumatic Fever in Relation to the Family and Environment

John R. Paul, M.D.

This paper is concerned with some of the local circumstances under which rheumatic fever has been found in the city of New Haven. It discusses its mode of spread through families, as an epidemic and an endemic disease, together with the different rates at which rheumatic manifestations occur in control families as opposed to rheumatic families with or without parental rheumatism.

Evidence is presented to show that the urban (local geographical) distribution of rheumatic fever indicates that it is a "crowd disease" and, to some extent, a disease of the poorer classes, simulating tuberculosis in this respect. Its seasonal and annual distribution parallels that of acute hemolytic streptococcus infections.

Communities are known to exist in this city where the prevalence of rheumatic fever is high. No adequate explanation of this high prevalence has been found, but some of the characteristics of these "rheumatic communities" are also discussed.

Poliomyelitis

James D. Trask, M.D.

The paper describes a few families in which there was poliomyelitis and in which attempts were made to recover the virus from the sick and healthy members. The results were that an example of a healthy carrier and some examples of abortive poliomyelitis were identified thereby.

In the second part of the paper the situations are enumerated where the virus has been detected in sewage.

The Use of Physical Therapy in Pediatric Patients

Muriel Case Downer, M.D.

Approximately 90 per cent of physical therapy consists of heat, massage, and exercise. By light therapy is meant the use of infrared, luminous, and ultraviolet radiations for therapeutic purposes. There are two groups of infrared radiations, the penetrating and the nonpenetrating. Penetrating infrared rays are emitted by all incandescent bodies such as the sun and incandescent lights. Nonpenetrating rays are emitted by all heated bodies which do not give out light, such as hot-water bottles, electric pads, and infrared generators.

Heat is of value in relieving certain forms of pain. When an area of the body is exposed to heat, the blood vessels dilate, there is an increase in circulation to the part, and recovery is hastened. For some types of cases the whirlpool bath and the paraffin bath have undoubted advantages.

Ultraviolet rays penetrate the skin to a very limited extent. Window glass and impurities in the air filter out the most effective rays of the sun.

Ultraviolet causes changes within the skin which affect the body's ability to utilize calcium and phosphorus. Certain rays produce redness of the skin, others tanning, and still others may kill various kinds of bacteria.

In administering light therapy, it should be remembered that if the distance from the source is decreased one-half, the intensity is increased four times. To be most effective, the light rays should strike the surface at a perpendicular angle. In general, ultraviolet is of value in the treatment of most forms of tuberculosis except pulmonary tuberculosis. It is of definite value in the prevention and treatment of rickets and in the treatment of a few skin conditions. According to the Council on Physical Therapy, the claim that exposure to ultraviolet rays increases or improves the tone of the tissues of the body as a whole, stimulates metabolism, or tends to prevent colds in normal persons has not been substantiated.

There are two possible effects of any massage movement, reflex and mechanical. The reflex effect is sedative and frequently relieves pain and muscle spasm. The mechanical effect assists the circulation of the blood and lymph; it may loosen adhesions and stretch contractures. Massage has a definite place in the treatment of infantile paralysis, nerve injuries, and numerous other conditions.

Therapeutic exercise is defined as supervised bodily movements with or without apparatus, for the purpose of restoring function to diseased or injured tissues and for maintaining normal function.

Exercise increases the heart beat, respiration, and circulation. Because of these actions it aids in carrying away waste products and in increasing the blood supply to the part. In passive exercise the patient must be relaxed while the operator moves the part through the range of motion. This maintains suppleness of the joints and helps to prevent adhesions and contractures. In active exercise, the patient must perform the exercise himself. Early in the treatment the patient may have assistance from the operator, but as the muscles become stronger, the patient performs these motions alone and finally is able to do them against the resistance offered by the operator. Nothing but active exercise will increase the strength of a muscle. It is upon this basis that we treat the weakened muscles of infantile paralysis and other conditions.

Diathermy, either conventional or short-wave, has but little use in pediatric practice. The chief objection to its use lies in the danger of causing burns. Movement of the child after application of the electrodes is apt to dislodge the electrode, with a resulting burn. At the present time there is no satisfactory way of measuring dosage; skin sensation is the only guide.

The galvanic current may be used in copper iontophoresis for the treatment of ringworm of the hands and feet. Electrical muscle stimulation is probably not indicated in weakened and paralyzed muscles. Recent work indicates that nerve injuries make a quicker recovery if only heat, massage, and exercise are used.

A Community Program for the Care of Crippled Children in New York City

Vernon W. Lippard, M.D.

In 1938 and 1939, an official commission appointed by the mayor of the city of New York conducted a survey of the crippled children of New York City and the facilities available for their care, as a basis for a coordinated program.

During a period of nine months 16,731 crippled children were registered. Thirty-three per cent had been disabled at birth by birth injuries or congenital abnormalities.

Infantile paralysis accounted for 29 per cent; sixty-nine per cent of those crippled as a result of infantile paralysis were afflicted before their fifth birthdays. Therefore, it is apparent that major emphasis should be placed on detection and treatment of these children during the preschool period.

Studies were made of hospital and convalescent home care, home nursing, social service, education, vocational training, and public health procedures. On the basis of recommendations made as a result of these studies, a Division of Crippled Children has been organized in the Department of Health and many other improvements in the facilities for the care of these children are in progress. Particular attention is being given to the inauguration of special clinics and educational and institutional facilities for the rehabilitation of children suffering from cerebral palsy (spastic paralysis).

One of the outstanding deficiencies in the program for the care of these children was found to exist in the field of vocational counselling. Very few boys and girls of high school age had received vocational guidance at a time when their ambitions were not too definitely crystallized and before they had been exposed to the shocks which are likely to occur when they discover that their education has not afforded them means of gaining a livelihood.

The results of the survey upon which this report is based have been published by the Commission for Study of Crippled Children as a monograph entitled "The Crippled Child in New York City."

Treatment of Certain Congenital Deformities in Children

Alexander L. Bassin, M.D.

The various factors which influence the development of certain imperfections of form and function present at the time of birth of a child may be due either to mechanical agencies derived from the uterus or to various alterations in the germ plasm or gene complexes. The latter concept appears more likely since defects have been observed in fetuses before the period when mechanical agencies can become active.

The factor of hereditary influence bears some effect upon the character of an anomaly or deformity. In spite of the fact that the development of these abnormalitis is beyond anticipation or control, their presence at the time of birth of the child raises the immediate important question of the future effect these anomalies may have upon the function of the organism. The estimate of the future can be based upon a careful analysis of the defects which are present, so that a reasonable outline of the optimum time for the beginning of treatment may be prepared.

The relative incidence of congenital anomalies and deformities has been variously estimated by numerous observers as being approximately 0.3 per cent. The incidence of specific anomalies, such as wryneck, has been estimated by Howell as being 1 in 150,000 births.

It is the purpose of this discussion to review several of the more common types of congenital anomalies, such as congenital clubfoot, congenital dislocation of the hip, congenital torticollis or wryneck, and deformities and anomalies of the spinal column. The numerous other types of anomalies and deformities, such as clubhand, congenital bridging of the bones, syndactylism or web fingers, congenital elevation of the scapula or shoulder blade, absent portions of members and extra digits, are in comparison quite small; even though they are excluded from this discussion, no effort is made to underestimate their significance in regard to treatment.

The review of numerous works on the subject of the diagnosis and treatment of congenital anomalies and deformities has shown a definite trend toward more skillful diagnosis of these defects in early life and has, therefore, enhanced the results of treatment. The fundamental concept evolved from the grouping of the

above anomalies and deformities is that conservative closed manipulative methods can be applied successfully to the correction of both form and function in a great number of cases. The utilization of conservative methods in the treatment of the clubfoot deformity, for example, has proved most effective in the reduction of this deformity in a large percentage of cases, particularly if this method is instituted early in the life of the child and continued until well after the period of active walking. The incidence of relapse of the correction is small, and the tendency of this recurrence of the deformity is greater in those cases in which evidence of other nerve damage had also been present; but for these cases the further application of open surgical treatment can then be relied upon to insure satisfactory control of the deformity.

Likewise, the results in the treatment of congenital dislocations of the hip and muscular wryneck parallel those obtained in the treatment of the congenital clubfoot. Early manipulative treatment is begun in these cases, often from the day of birth, and the corrected position is controlled by restraining appliances. Here, also, following a reasonable trial of conservative measures, open surgical treatment can be adopted to secure further restoration of form and function.

The type of case which requires more persistent and prolonged care by conservative measures before surgical interference can be utilized is the child in whom anomalies of the vertebrae are present. The progress made in the treatment of this group of cases indicates that open surgical procedures are being postponed until a sufficient trial by manipulation and appliances has been attempted.

Reports from various clinics throughout the country confirm the general consensus that the prognosis from the treatment of these types of congenital anomalies and deformities is good. A higher level of uniformly good results can be reached when the diagnosis is made early and treatment started promptly.

The Cerebral Palsies

Winthrop Morgan Phelps, M.D.

The term "cerebral palsies" has been adopted to cover all disturbances of the brain affecting the motor system as a result of congenital, birth, or acquired lesions. The term supplants to a great extent "spastic paralysis" since spasticity is only one of the conditions resulting from brain damage and it is therefore very confusing to use this term to cover the entire field.

In the interests of accurate diagnosis as a basis both for treatment and for pathologic study, careful subdivisions of cerebral palsy must be made into different entities which can be recognized. The relationship of surgery, physical retraining, and drug therapy to these conditions varies widely, and a discussion will be made of the indications for the use of these measures in relation to each entity.

Associated sensory handicaps of sight and hearing play an important part in these conditions and must be recognized in relation to the total picture in order to avoid inaccurate mental evaluation.

The following papers constituting a symposium on "Certain Problems of Puberty and Adolescence" will be published in a later issue of the JOURNAL.

General Considerations. Lawrence K. Frank.
Some Observations on the Growth and Development of Adolescent Children. William W. Greulich, Ph.D.
Obesity in Relation to Puberty. Hilde Bruch, M.D.
Gynecologic Problems of Adolescence. Arthur H. Morse, M.D.
Endocrine Therapy. Ephraim Shorr, M.D.
Psychiatric Considerations. Douglas A. Thom, M.D.

TREASURER'S REPORT

Statement of Receipts and Disbursements

July 1, 1940, to June 30, 1941

Balance, July 1, 1940			$ 8,872.12
Receipts:			
Dues		$26,421.35	
Exhibits, 1940 Meeting	$2,832.50		
Exhibits, 1941 Meeting	4,037.50	6,870.00	
Interest on bonds		656.21	
Transferred from Council for Pediatric Research to General Fund		212.19	
International Congress of Pediatrics		110.00	
Pamphlets:			
Child Health Record	$ 591.20		
Immunization Procedures	462.15		
Vitamins	43.10	1,096.45	35,366.20
			$44,238.32
Disbursements:			
Salaries:			
Secretary	$7,500.00		
Assistant Secretary	1,200.00		
Stenographer	2,000.00		
Office	566.50	$11,266.50	
Rent		1,200.00	
Subscriptions		6,281.51	
Annual Meeting, 1940	3,606.99		
Annual Meeting, 1941	243.16	3,850.15	
Publicity		3,807.20	
Executive Board		2,957.39	
Stationery and Printing		850.99	
Office Supplies and Equipment		735.28	
Postage		647.90	
Travelling Expense (Secretary)		567.26	
Telephone and Telegrams		261.64	
Charge and Exchange on Checks		137.86	
Certificates and Mounting		107.52	
Treasurer's Bond		62.50	
Refund—Initiation Fee		25.00	
Miscellaneous		130.76	
Pamphlets:			
Child Health Record	$ 461.70		
Immunization Procedures	627.15		
School Health	2.90		
Vitamins	332.77	1,424.52	
Expense:			
Committee	1,478.37		
State	682.94		
Regional	260.88	2,422.19	
International Congress of Pediatrics		220.00	36,956.17
Balance, June 30, 1941			$ 7,282.15

Audited and found correct.

Academy News

Since the American Academy of Pediatrics established the Committee on Central and South American Scholarships in November, 1939, this Committee has approached several university foundations and large industrial concerns who have generously granted eight scholarships for South and Central American Pediatricians. The grantors are: Mead Johnson & Company, the foundations of the University of Chicago and the University of Cincinnati, the Mayo Foundation, Abbott Laboratories, The Quaker Oats Company, M and R Dietetic Laboratories, Inc., and the Wisconsin Alumni Research Foundation. These scholarships consist of $1,200 a year and are available for three years.

The following universities have expressed their willingness to take the candidates: Johns Hopkins University, Harvard University, University of Chicago, University of Minnesota, Chicago Children's Hospital, University of Cincinnati, Mayo Clinic, University of Iowa, Western Reserve University, Yale University, University of Illinois, University of Wisconsin, Vanderbilt University, University of California, and the University of Rochester.

As soon as these scholarships were procured, the Committee approached the national pediatric societies of the following countries: Cuba, Mexico, Chile, Brazil, Uruguay, Argentina, and Venezuela. It was suggested that each national pediatric society appoint a committee which would take charge of the selection of the most suitable candidate. Up to the present time, the following committees on Latin-American Scholarships have been appointed:

Mexico

President: Dr. Enrique Baz-Dresch
Members: Dr. Jesús Lozoya
Dr. Roberto L. Sanchez
Annual Secretary of the Mexican Society of Pediatrics: Dr. Luis Berlanga Berumen

Argentina

President: Dr. Ramon R. Arana, Director of the Childrens' Hospital of Buenos Aires and Actual President of the Argentine Pediatric Society
Members: Prof. Mamerto Acuña, Bs. As., Professor of Pediatrics
Prof. Pedro de Elizalde, Bs. As., Professor of Pediatrics
Prof. Raul Cibils Aguirre, Bs. As., Director of Public Assistance
Dr. Fernando Schweitzer, Professor of Pediatrics in La Plata
General Secretary of the Argentine Pediatric Society: Dr. Alfredo E. Larguía

Cuba

President: Prof. Angel A. Aballí, Professor of Pediatrics at the University of Habana
Members: Prof. Clemente Inclan, Professor of Experimental Pathology at the University of Habana
Prof. Agustin Castellanos, Assistant Professor of Pediatrics
Prof. Teodosio Valledor, Assistant Professor of Pediatrics
Secretary: Dr. Serafin Falcón, Secretary of the Cuban Society of Pediatrics
Advisor: Dr. Henry P. Carr, Rockefeller Foundation

Chile

Dr. Gonzalo Moraga Fuenzalida, Ex-President of the Chilean Pediatric Society
Dr. Adalberto Steeger

Dr. Manuel Muñoz, Vice-President of the Chilean Pediatric Society
Dr. Agustin Inostrosa, President of the Chilean Society of Pediatrics
Dr. Joaquin Luco, Representative of the Guggenheim Foundation

Venezuela

Dr. Pastor Oropeza, Director of the Venezuelan Archives on Child Health and Pediatrics
Dr. Gustave H. Machado, Ex-President of the Venezuelan Society on Child Health and Pediatrics
Dr. Espíritu Santos Mendoza, Chief of the Division on Maternal and Child Health of the Ministry of Hygiene and Public Health
Dr. Ernesto Vizcarrondo, Actual President of the Venezuelan Society on Child Health and Pediatrics

Recently the Mexican Committee informed the Committee on South and Central American Scholarships in this country that they have selected Dr. Fernando Madero G. for the scholarship. Dr. Madero is now beginning his work in the Pediatric Department of the Bobs Roberts Memorial Hospital in Chicago.

The Chilean Committee has appointed Dr. Julio Meneghello, who, it is hoped, will begin his work with the academic year in September.

News and Notes

The University of Pennsylvania Bulletin of the Graduate School of Medicine announces plans and arrangements for the session of 1941-1942. An important part of the Graduate School is the work in pediatrics for graduate students doing University work. Dr. Howard C. Carpenter, 1805 Spruce St., Philadelphia, is Vice-Dean of Pediatrics, and inquiries should be addressed to him.

The dates for the 1942 spring examinations by the **American Board of Pediatrics** have not yet been determined, but the locations will be as follows:

Philadelphia, Pa.—At the time of the meeting of Region I of the American Academy of Pediatrics, probably in March or April.

Cleveland, Ohio—At the time of the meeting of Region III of the American Academy of Pediatrics, probably in May.

Los Angeles, Calif.—At the time of the meeting of Region IV of the American Academy of Pediatrics, probably in May.

A "Mothers' Charter," designed to summarize the minimum demands made on society by the mothers of its children, was made public by the **American Committee on Maternal Welfare,** central organization of the country's obstetricians, gynecologists, nurses, and hospital and public health leaders in the fight to reduce maternal and infant mortality.

The charter, drafted by Dr. Fred L. Adair, of Chicago, chairman of the committee, was printed for the first time in "The Mother," its quarterly magazine. It complements the "Children's Charter" drawn up in 1934 by the famous White House Conference on Child Health and Protection, and together the two "charters" stand as the general objective of the organization.

In the intense concentration of the nation's resources on the needs of defense, the committee believes there is danger that the long fight to preserve the lives of

American mothers and babies may lose its momentum. In the last few years the maternal and infant death rates in the United States have been brought down to record low levels, and the committee considers it essential to hold these gains.

Here is the new "charter" of American motherhood:

THE MOTHERS' CHARTER

Every potential mother envisions the pleasures and obligations of creating and sustaining new life and is entitled to health and protection for the benefit of herself and humanity and she should have:

1. The inherent right to be well born without inherited or transmitted defect or disease.
2. The inalienable right to protection from disease and harmful influences.
3. The opportunity to learn and know herself during adolescence and maturity and to acquire a knowledge of the origin and significance of human life.
4. The right to protection from pitfalls of married life and to a knowledge of its significance to herself and her potential family.
5. The privilege of proper premarital and preconceptional medical examination and advice and care for herself and her mate.
6. The right of proper and adequate care during pregnancy.
7. The right to receive adequate and necessary care during labor in her home or hospital.
8. The right to have appropriate care following labor in her home or hospital.
9. The right to secure proper and continuing subsequent care for herself and baby.
10. The right of preservation of health and life and happiness for herself and family.

The American Committee on Maternal Welfare is composed of the following organizations:

American Association of Obstetricians, Gynecologists, and Abdominal Surgeons
American College of Surgeons
American Gynecological Society
American Hospital Association
American Protestant Hospital Association
Section on Obstetrics and Gynecology of the American Medical Association
American Medical Women's Association
American Nurses Association
American Public Health Association
Catholic Hospital Association
Central Association of Obstetricians and Gynecologists
Chicago Maternity Center
Maternity Center Association of New York
National League of Nursing Education
National Medical Association
National Organization for Public Health Nursing
New England Obstetrical and Gynecological Society
Pacific Coast Society of Obstetrics and Gynecology
Southern Medical Association
U. S. Bureau of the Census
U. S. Children's Bureau
U. S. Public Health Service
Frontier Nursing Service
American Social Hygiene Association

Book Reviews

Biologic Fundamentals of Radiation Therapy. F. B. Ellinger. New York, 1941, Nordeman Publishing Co., Inc. Price $5.00.

Translated from the German edition published five years earlier, the book presents an extensive review of experimental radiation biology. An introductory section is given on the nature of the problems involved, but, if uninitiated, the reader will do well to familiarize himself first with the physical principles of radiation treatment. The effects of electromagnetic radiations on different tissues are given in detail. The discussion not only includes roentgen and gamma rays, but also ultraviolet, infrared, and visible light. The action of particle radiations is described. The book presents a broad foundation for knowledge of radiosensitivity and biologic factors responsible for tissue changes following the administration of radiation. The data on experimental work are closely integrated with clinical practice, but some may be of the opinion that the author has attempted a degree of precision in that correlation not attained therapeutically. A remarkably complete bibliography is given with many foreign references that may have escaped readers on this subject.

A. N. A.

Community Organization for Health Education. New York, 1941, American Public Health Association. Price $0.09.

This is an interesting report of a special committee of the American Public Health Association financed by a fund of the Massachusetts Institute of Technology. The committee, headed by Prof. C. E. Turner, studied and reported on the programs of ten counties in a number of states and on two state programs. In general, the committee finds there is no single best plan, but the plan must be determined by local conditions. More important than the plan is the personnel in charge.

School Health Service. W. Frank Walker and Carolina R. Randolph. New York, 1941, Commonwealth Fund. Price $1.50.

The authors present a study of the school health program in six Tennessee counties where the school health program has been conducted by a full-time public health agency. The study includes 58,000 children over a span of six years. In general, the conclusions of the survey are that a program should not be fixed or static but should be one that evolves with community development.

The study shows that a much greater percentage of correction of the defects found on examination takes place when the parent is present at the examination; the use of some form of award, such as a badge, is helpful in obtaining results; preschool supervision is of distinct value in lessening the amount of certain defects such as dental caries but does not change the nutritional defects to any extent; repeated or multiple examinations have little effect on the correction of defects, except those of vision; there is little value in the examination itself in judging serious tonsil defects.

The study is important for all interested or engaged in public health programs and for pediatricians engaged in school work.

How to Raise a Healthy Baby. L. J. Halpern, M.D. New York, 1940, Prentice-Hall, Inc., pp. 388. Price, $1.95.

This work is another addition to the never-ending number of books on the care of the baby for lay readers. The usual field is covered, and, in general, it is neither better nor worse than the average. The material is presented in the method of a catechism rather than in a direct discussion and the answers, as a rule, are clear and direct. The method necessarily imposes at times a definite answer to a subject that is by no means clear or definite medically.